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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 158 and 161

[EPA-HQ-OPP-2008-0110; FRL-8886-5]

RIN 2070-AD30

Data Requirements for Antimicrobial Pesticides

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is revising the data requirements for antimicrobial pesticide products to reflect current scientific and regulatory practice, and to provide the regulated community with clearer and transparent information about the data needed to support pesticide registration decisions for antimicrobial products. The updated data requirements also serve to further enhance EPA's ability to make regulatory decisions about the human health, and environmental fate and effects of antimicrobial pesticide products. These revisions are also expected to help protect human health and the environment by providing an up-to-date scientific framework for identifying and assessing the risks of antimicrobial pesticides sold or distributed in the United States.

DATES: This final rule is effective [*insert date 60 days after date of publication in the Federal Register*].

ADDRESSES: The docket for this action, identified under docket identification (ID) number EPA-HQ-OPP-2008-0110, is available at <http://www.regulations.gov> or at the OPP Docket in the Environmental Protection Agency Docket Center (EPA/DC), located in the EPA West Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805. Please review the visitor instructions and additional information about the docket available at

<http://www.epa.gov/dockets>.

FOR FURTHER INFORMATION CONTACT: Kathryn Boyle, Field and External Affairs Division (7506P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 305-6304; e-mail address: *boyle.kathryn@epa.gov*, or contact Scott Drewes, same address: telephone number (703) 347-0107; email address: *drewes.scott@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. Executive Summary

A. Does this Action Apply to Me?

You may be affected by this action if you are a producer of pesticide products (NAICS 32532), antifoulants (NAICS 32551), antimicrobial pesticides (NAICS 32561) or wood preservatives (NAICS 32519), importers of such products, or any person or company who seeks to register an antimicrobial, antifoulant coating, ballast water treatment, or wood preservative pesticide or to obtain a tolerance for such a pesticide. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed could also be affected.

B. What is the Agency's Authority for Taking this Action?

This action is issued under the authority of sections 2, 3, 4, 5, 10, 12, and 25 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 U.S.C. 136 *et seq.*, and section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a. The data required for antimicrobials (e.g., for registration, reregistration or registration review, experimental use permit (EUP), or tolerance/tolerance exemption) are currently listed in 40 CFR part 161 and, with this final rule, will be listed in 40 CFR part 158.

C. What Action is the Agency Taking?

The Agency is revising and updating the data requirements for antimicrobial pesticides that are currently found in Title 40 of the Code of Federal Regulations (CFR) in part 161, and which are being relocated as revised by this rule to subpart W of part 158. Subpart W sets out data requirements specific to antimicrobial products that are described by the antimicrobial use patterns and use exposure considerations particular to antimicrobials. With the promulgation of part 158, subpart W, EPA is removing part 161, entitled “Data Requirements for Registration of Antimicrobial Pesticides” as it is no longer needed.

Antimicrobial pesticides are used to control microbiological contamination in healthcare applications, and deterioration in industrial, commercial, and consumer products. Nearly 60 percent of antimicrobial products are registered as public health products (as defined at FIFRA 2(gg)) to control infectious microorganisms in hospitals and other health care environments. Public health products are intended to control microorganisms infectious to humans in any inanimate environment. The common public health antimicrobial products include sterilants, disinfectants, and sanitizers. Nonpublic health products are sold and distributed for use to control growth of algae, odor-causing bacteria, bacteria which cause spoilage, deterioration or fouling of materials and microorganisms infectious only to animals. Other examples of nonpublic health products include products used in cooling towers, jet fuel, paints, and treatments for textile and paper products. Within this final rule EPA is using the term antimicrobials to collectively refer to antimicrobial pesticides, antifoulant coatings and paints, and wood preservatives. The amendments contained in this final rule, which are discussed in detail in Units IV. through XXII. of this document, change the existing data requirements for antimicrobial pesticides in the following substantive respects:

- By changing some of the existing data requirements, such as a change from

conditionally-required to required, a change in the number of test species, or expanding the number of use patterns for which the test is required.

- By adding newly codified data requirements, i.e., data requirements that are not currently identified in 40 CFR part 161, but are considered in current practice on a case-by-case basis.

- By adding new data requirements, i.e., data requirements that have not been required or have rarely been required in current practice on a case-by-case basis, and have not been routinely considered during the Agency's evaluation of the data needed for the purpose of risk assessment.

- By eliminating the requirement for the chronic non-rodent study currently required in 40 CFR part 161.

- By codifying the antimicrobial data requirements as finalized in this rule in 40 CFR part 158, subpart W, and removing the current requirements that appear in 40 CFR part 161.

D. What are the Incremental Costs and Benefits of this Action?

The Economic Analysis (EA) of the potential costs and benefits associated with this action, as revised to address comments received on the proposed rule, is contained in a document entitled "Final Economic Analysis of Changes in Data Requirements for Antimicrobial Pesticides" (Ref. 1), a copy of which is in the docket, discussed in Unit XXII., and are briefly summarized here.

1. *Estimated costs.* In its analysis, the Agency considered the potential, additional costs for the registration of new antimicrobial pesticides or new uses of currently registered antimicrobial pesticides, as well as the potential, additional costs incurred during the registration review of existing antimicrobial pesticides.

The estimated total annual industry costs of the final rule is expected to be about \$19.3 million. The difference between the baseline costs (the existing data requirements

that were codified in 1984) and the cost of the Agency's current practices is about \$1 million annually. The difference between the baseline costs and the final rule costs, i.e., the incremental costs, is approximately \$8.2 million annually assuming an estimated 15 new registrations.

Under the final rule, the average cost per registration action of a new antimicrobial active ingredient is approximately \$1 million to \$5 million. For existing chemicals, data requirements in part 158, subpart W are relevant to the registration review program, and the average additional cost is estimated to be about \$588,000 for wood preservatives, \$284,000 for food and indirect food uses, and \$260,000 for all other uses. For registration review, the total annual cost is \$6.8 million.

EPA also conducted an analysis of the potential impact of this final rule on small entities, which is included in the EA and discussed in Unit XXV.C. In brief, EPA estimates that 500, or approximately 67 percent, of the unique parent companies that constitute the total universe of pesticide antimicrobial registrants, qualify as a small business. When considering both registration review and new registrations, on average each year about 30 small businesses are estimated to incur additional costs under this final rule. EPA estimates that about 23 small firms (almost 5 percent of the 500 small antimicrobial firms) may experience an economic impact of 3 percent or more of gross sales. As discussed later in this document, EPA has concluded, based on this analysis, that this potential impact is not a significant impact on a substantial number of small entities.

2. *Estimated benefits.* In its analysis, EPA provides a qualitative discussion of the benefits, which are not quantifiable in the same monetary terms as the costs. In general, before manufacturers can sell pesticides in the United States, EPA must evaluate the pesticides thoroughly to ensure that they meet Federal safety standards in FIFRA and FFDCA that were established to protect human health and the environment. EPA grants a "registration" or license that permits a pesticide's distribution, sale, and use only after the

company meets the scientific and regulatory requirements. In evaluating a pesticide registration application, EPA assesses a wide variety of potential human health and environmental effects associated with use of the product. Applicants, or potential registrants, must generate or provide the scientific data necessary to address the identity, composition, potential adverse effects, and environmental fate of each pesticide. The information provided by the data requirements in this final rule allow EPA to evaluate whether an antimicrobial pesticide meets the applicable statutory standards.

Antimicrobials play an important role in public health and safety. While intended to provide health benefits of pathogen control or removal and, in some cases, safety benefits of materials preservation, they also involve risks of potential efficacy failure and exposure of hazards to humans and the environment. Therefore, the effectiveness and proper use of an antimicrobial pesticide is determined by EPA based on its evaluation of specific data that is provided as part of registration and registration review activities.

This final rule will enhance EPA's ability to make sound regulatory decisions and help prevent the registration of pesticide products that may have unreasonable adverse effects on human health and the environment. The Agency believes that having the appropriate data ultimately leads to better risk management decisions, as well as provides the following other benefits:

i. *More refined assessments mean less uncertainty and clearer understanding of actual risks.* For example, EPA's current applicator/user exposure data base is not comprehensive, especially regarding exposures to pesticides in industrial and residential settings. Codifying these data requirements, many of which are currently applied on a case-by-case basis, would allow the Agency to conduct improved exposure assessments for applicators/users. This will benefit workers and consumers by allowing EPA to make better informed regulatory decisions that are neither too stringent nor too lenient.

ii. *Clarity and transparency to regulated community means savings.* The enhanced

clarity and transparency of the information presented in part 158, subpart W will reduce uncertainty for applicants in generating and submitting data that is necessary for EPA to be able to make registration decisions based on data-driven risk estimates that use fewer conservative assumptions. Applicants may save time and money by understanding which studies are needed to support the use of their product. Thus, the antimicrobial industry will, along with other partners in the regulated community, attain a better understanding of and can more efficiently participate in the pesticide registration process. This should allow products to enter the market earlier, thereby enabling registration of safer pesticides sooner and potentially reducing risks, as well as increasing profits. The clarity derived from having data requirements specific to antimicrobials may be especially important to small firms and new firms entering the industry who may have less experience than those firms that routinely work with the Agency.

iii. *EPA information assists other communities in assessing pesticide risks.*

Scientific, environmental, and health communities find pesticide toxicity information useful to respond to a variety of needs. For example, medical professionals are concerned about the health of patients exposed to pesticides; poison control centers make use of and distribute information on toxicity and treatment associated with poisoning; and scientists use toxicity information to characterize the effects of pesticides and to assess risks of pesticide exposure. Similarly those responsible for protection of nontarget wildlife need reliable information about pesticides and assurance that pesticides do not pose an unreasonable threat. These data requirements will help the scientific, environmental, and health communities by increasing the breadth, quality, and reliability of Agency regulatory decisions by improving their scientific underpinnings.

iv. *Better informed users mean informed risk-reduction choices.* Better regulatory decisions resulting from these data requirements also mean that the label will provide better information on the use of the pesticide. A pesticide label is the user's direction for

using pesticides safely and effectively. It contains important information about where to use, or not use, the product, health and safety information that should be read and understood before using a pesticide product, and how to dispose of that product. This benefits users by enhancing their ability to obtain pesticide products appropriate to their needs, and to use and dispose of products in a manner that is safe and environmentally sound.

v. *Recognizes the unique down-the-drain uses associated with antimicrobials.* For antimicrobial chemicals that go down the drain and eventually reach a waste water treatment plant (WWTP), EPA intends to conduct an assessment of the potential impact of the antimicrobial chemical on the microorganisms in the biological treatment processes of a WWTP and the potential for the antimicrobial chemical to pass through the WWTP in the effluent. The final rule will minimize costs to States and municipalities by ensuring that antimicrobial pesticide products registered under FIFRA don't cause water quality problems or harm treatment facilities.

vi. *A milestone towards the Agency's vision for 21st Century toxicology and new integrated testing strategies.* The Agency's goal is to use 21st Century science to increase the efficiency and effectiveness of our assessment process. This rule is a launching pad for that vision.

II. Background

A. Brief History of Pesticide Data Requirements

EPA's data requirements for pesticides were first published in 1984. Those data requirements were primarily influenced by agricultural uses. Since then, new risk concerns have been identified, and EPA's statutory mandates for pesticide registration under FIFRA and tolerance-setting under the FFDCA were amended in 1996 to require EPA to update the scientific underpinnings of risk assessments. The Agency must now perform more in-depth risk analyses, such as aggregate and cumulative risk assessments.

On October 26, 2007, EPA promulgated final rules updating the data requirements for conventional pesticides (72 FR 60934), and biochemical pesticides and microbial pesticides (72 FR 60988). The rule development process for part 158, subpart W used the updated conventional pesticides data requirements as the starting point while considering the case-by-case data requirement decisions made over the years of registering antimicrobial pesticide products. The following four subparts in part 158, promulgated in 2007, also apply to antimicrobial pesticides (see 40 CFR 158.1):

- Subpart A: General Provisions
- Subpart B: How to Use Data Tables
- Subpart C: Experimental Use Permits
- Subpart D: Product Chemistry

To provide continued regulatory coverage for antimicrobial pesticides until the Agency could promulgate a final regulation for antimicrobial pesticides, the 2007 final rule (72 FR 60251, October 24, 2007) (FRL-8116-2) preserved the original part 158 data requirements (promulgated in 1984) to apply to antimicrobial pesticides by redesignating them as part 161. This final rule finishes the promulgation of a final regulation for antimicrobial pesticides. Accordingly, EPA is also revoking 40 CFR part 161.

B. How to Use the Data Tables

In establishing the data requirements in 1984, EPA adopted a step-wise approach to assist the applicant in determining the data needed to support the registration of a particular product. This approach, which is described in 40 CFR part 158, subpart B, involves the use of “data tables” to facilitate the identification of the applicability of the data requirements. In essence, the data requirements illustrate the questions the registrant will need to answer about the safety of the pesticide product before the Agency can register it. Because of the variety of chemicals and use patterns, and because EPA must retain flexibility to tailor data

requirements as appropriate, only qualitative descriptors are in the tables. Test notes provide more specific information on the applicability of specific data requirements.

The table descriptors NR (not required), R (required), and CR (conditionally required) should be viewed as a general presentation, indicating the likelihood that the data requirement applies. The use of R does not necessarily indicate that a study is always required, but that it is more likely to be required than not. For example, if the applicant wanted to apply his pesticide to apples, then crop field trials would be required almost always on apples. However, if the physical/chemical properties of the chemical did not lend themselves to the test, such as performing an inhalation test with a chemical that is a solid and has an extremely low vapor pressure, then a waiver might be granted. Generally, test notes for R studies discuss any particular circumstances when the testing might not be required.

The use of CR means a study is less likely to be required. Triggers in the test notes indicate the circumstances under which the Agency has learned through experience that the information is needed. Although only an approximation, if percentages were to be assigned to indicate the need for a particular study, then R could be viewed as representing the submission of a study 50 to 100 percent of the time and CR would be up to 50 percent

Thus, NR, R, and CR are used for convenience to make the table format feasible, but serve only as a general indication of the applicability of a data requirement. In all cases, the test notes referred to in the table must be consulted to determine the actual need for the data.

The table format includes a column heading entitled "Guideline," which refers to the OCSPP Harmonized Test Guidelines. Guideline numbers are provided as information/guidance to applicants. These Guidelines set forth recommended instructions and test methods for performing a study to generate the required data. Since these are guidance documents, the applicant is not required to use these Guidelines, but, may instead

seek to fulfill the data requirement by other appropriate means, such as alternative test methods, submission of an article from open literature, or use of modeling. The applicant may submit a protocol of his own devising for the Agency to review. However, the OCSPP Harmonized Guidelines have been developed through a rigorous scientific process, including extensive peer review by the Advisory Panel (SAP). Additionally, many of the Guidelines have been harmonized internationally. As such, they represent the recommended approach to developing high-quality data that should satisfy EPA's data needs for risk assessment.

In addition, since it is not possible to sufficiently delineate all circumstances in test notes, consultation with EPA is encouraged. Applicants are also encouraged to visit the Agency's website at http://www.epa.gov/pesticides/regulating/data_requirements.htm.

C. Efforts to Incorporate 21st Century Science into Pesticide Decision Making

Over the next several years, EPA's Office of Pesticide Programs (OPP) is committed to improving and transforming the Agency's approach to pesticide risk management by enhancing the Agency's ability to use integrated approaches to testing and assessment. The Pesticide Program plans to maximize use of existing data from similar compounds, including information from new *in silico* and *in vitro* predictive models and exposure modeling to target *in vivo* toxicity testing that is needed to assess and manage chemical risks appropriately.

Over the next decade, as experience is gained and as the Agency's understanding of toxicity pathways increases, an enhanced integrated testing and assessment approach will be implemented for all pesticides. The approach will fully integrate hazard and exposure information using advanced computer modeling of new *in vitro* data and an understanding of toxicity pathways to better predict risks and to determine what additional data are necessary to provide a sound basis to manage risks of concern. Data from improved biomarkers of exposure and biological outcomes from population-based studies will be

used to evaluate the effectiveness of this new risk assessment paradigm, to readily identify early effects in exposed populations, and to improve the approach.

Current Agency scientific and regulatory practice provides the foundation for this final rule. While current practice is still largely dependent on animal (*in vivo*) testing, this rule is one milestone towards the Agency's longer term vision for 21st Century Toxicology and new integrated testing strategies. OPP believes that certain classes of chemicals, such as antimicrobial pesticides, provide an appropriate starting point for OPP's planned transformation. Many antimicrobials have both pesticidal and non-pesticidal uses. In addition, many antimicrobial products are regulated under multiple jurisdictions. Thus, many antimicrobial chemicals have been assessed by other regulatory programs and agencies. The ready availability of published literature and publicly-available assessments offer a unique opportunity for the applicant to use the available information as a starting point for fulfilling data requirements, and, when appropriate, to use computer modeling and/or *in vitro* data to supplement or fulfill data requirements. For example, OPP established a voluntary pilot program for eye irritation testing of certain antimicrobial pesticides using non-animal test methods. OPP will continue to evaluate use of new *in vitro* and computer-based approaches in OPP's hazard and risk assessment processes as the technologies are sufficiently developed and peer-reviewed. Certain tools are already available or anticipated to become available in the near term including, (Quantitative) Structure-Activity-Relationship (Q)SAR/expert systems and *in vitro* high through-put screening technologies. Furthermore, in conjunction with the International Life Sciences Institute (ILSI), OPP is currently pursuing the development of an application of the thresholds of toxicological concern (TTC) concept to evaluate antimicrobial pesticides. In collaboration with OPP, EPA's Office of Research and Development (ORD) is providing momentum for achieving the vision of 21st Century Toxicology by developing and evaluating new technologies in molecular, cellular, and computational sciences to

supplement or replace more traditional methods of data development. OPP believes that its goal of using 21st Century science in integrated approaches to testing and assessment is achievable with strong scientific and stakeholder support through a transparent process. As the enhanced integrated testing and assessment approach matures, based on these scientific advances, EPA may determine to update its data requirements to reflect evolving program needs as specified in § 158.30(c). See Unit XVIII. of the proposed rule for further discussion of EPA's use of integrated approaches to testing and assessment.

III. Public Comments on the Notice of Proposed Rulemaking (NPRM)

A. Comments Submitted to EPA

This unit discusses, in general terms, the public comments received on the NPRM that appeared in the **Federal Register** of October 8, 2008 (73 FR 59382), and EPA's responses to those comments. The comment period for the NPRM was extended from January 6, 2009 to April 6, 2009, to allow stakeholders additional time to submit their comments. In addition, EPA convened a public workshop in Arlington, Virginia, to explain the provisions of the NPRM on November 6, 2008. The proposed rule, the notice of the extension of the comment period, the notice of the public meeting, the presentations used at the public meeting, the comments submitted, and EPA's Response to Comments Document are available in the docket for this rule.

During the public comment period, EPA received comments on the proposed part 158, subpart W regulations from 29 entities. There were also late comments received at meetings held at EPA in Arlington, VA on December 2, 2009, and June 14, 2010, as well as at a meeting on May 17, 2011, and in a letter dated June 17, 2011. The presentation materials and EPA's summary of the meetings, and the letter with attachments are included in the docket. These late comments were not new comments, but rather restatements of issues presented in their original comments submitted to EPA, and are also available in the docket. Another late comment, received on September 1, 2010, was addressed by adding

additional comments and responses to the toxicology section of the Response to Comments Document.

EPA carefully reviewed all comments submitted, and provides responses in the Response to Comments Document, a copy of which is available in the docket. The Response to Comments Document also contains the rationale for the changes that were made from the proposed rule to the final rule, in response to submitted comments. Similar comments are grouped together. Comments that had a substantive impact on changes from the proposed rule to the final rule are also discussed in Units IV. to XXII. of this document.

B. Overview of this Final Rule

1. *In general.* This final rule reflects updates and revisions to the data requirements currently contained in 40 CFR part 161, in many cases by codifying the case-by-case data requirements decisions made over the years to help apply the agriculturally-based 1984 data requirements to antimicrobial pesticide products. The antimicrobial data requirements are being relocated to 40 CFR part 158, subpart W, and 40 CFR part 161 is being removed.

Based on comments received, EPA revised the proposed data tables. EPA's Response to Comments Document contains the rationale for the changes that were made from the proposed rule to the final rule in response to submitted comments.

Eleven new data requirements for antimicrobial pesticides are being codified in this final rule. As discussed in the preamble to the proposed rule, a "new" data requirement "means that the data requirement has never been required or has rarely been required on a case-by-case basis, and has not been routinely considered during the Agency's evaluation of the data needed for the purpose of risk assessment" (73 FR 59387). Eight new data requirements that were proposed in 2008 and are now being codified are: Developmental neurotoxicity; immunotoxicity; photodegradation in soil; soil residue dissipation; ready

biodegradability study; porous pot study; activated sludge sorption isotherm study; and modified activated sludge, respiration inhibition test. The developmental neurotoxicity and immunotoxicity tests are new compared to part 161, but were added for conventional pesticides in the 2007 amendments to part 158. The photodegradation in soil study was not previously required for wood preservatives. The other four studies are unique to antimicrobials.

Based on comments received, two other “new” data requirements are being added that serve as alternatives to tests that were proposed (and are now being finalized): Simulation tests to assess the biodegradability of chemicals in discharged wastewater, and simulation test – aerobic sewage treatment: Activated sludge units. Similarly, also based on comments, one “new” data requirement, the nature of the residue on surfaces, is being added as a more definitive trigger or screen for determining whether one of the studies that was proposed – the migration study – must be conducted.

Additionally, this final rule:

- Codifies data requirements/use pattern combinations that were not codified in part 161, but have typically been required to register an antimicrobial pesticide product.
- Provides improved definitions for antimicrobial pesticides used for public health and nonpublic health purposes.
- Codifies data requirements to determine risks to WWTPs and the potential for movement of antimicrobials and their degradates from the indoor environment to the outdoor environment via effluent discharge from a publically owned treatment work (POTW).

The data requirements promulgated in this final rule identify the types of information that EPA needs to determine whether an antimicrobial pesticide product should be registered and to make decisions regarding tolerances or tolerance exemptions

for pesticide residues in food. Subpart W to part 158 includes a series of tables and regulatory text that mirrors the structure of the data requirements for conventional pesticides. However, subpart W establishes specific data requirements for each scientific discipline (except product chemistry) for antimicrobial pesticides. As explained in Unit II.A. of this document, subpart D to part 158, which contains the product chemistry data requirements for conventional pesticides, also applies to antimicrobials. The order of subpart W also mirrors that of the larger part 158. As such, the following data requirements categories are included in detail in part 158, subpart W: Product performance, hazard/toxicity (both human health and ecological toxicity), exposure (both application and post-application human exposures), residue chemistry, and environmental fate requirements.

EPA is also codifying 12 antimicrobial use patterns, as described in the proposed rule (73 FR 59389, October 8, 2008). As part of this final rule, EPA has developed an Antimicrobial Use Site Index to provide additional information about these use patterns. This index is included in the docket and is posted on the Agency's website.

2. *Changes from what was proposed.* In response to comments, EPA has made numerous changes to the proposed requirements in crafting the final rule. The most significant changes are summarized as follows.

i. *Alternatives to the porous pot study.* With regard to the porous pot study in the final environmental fate data requirements table in § 158.2280, EPA is adding two simulation studies that can serve as an alternative to the porous pot study. This change was based on a comment that requested consideration of whether “studies that simulate wastewater treatment plants (WWTPs) [could] substitute for [the porous pot study].” (ACC Comment identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.9; Appendix H, entitled “Comments on Proposed Data Requirements for Environmental Fate” p. 5). Additionally, in the commenter's suggested environmental fate

data requirements table (p.11), instead of giving the title of the study as “Porous Pot,” the commenter wrote “Simulated WWTP; e.g., Porous Pot Study.”

EPA agreed with the commenter and identified two other studies: The biodegradation in activated sludge study as described in the OPPTS guideline entitled “Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater” and simulation test – aerobic sewage treatment: Activated sludge units. This change provides applicants with more flexibility in meeting this data requirement. EPA’s rationale is described in Unit XV.A., and for greater detail see response to comment 134.1 in the Response to Comments Document in the docket. Test note 3 to the final environmental fate data requirements table in § 158.2280 clearly specifies that only one biodegradation study is to be submitted.

In creating a tiered structure for the antimicrobial environmental fate data requirements table, the table and accompanying test notes are intended to be used to determine which antimicrobials would be expected to reach a WWTP. Test notes 18, 19, 20, and 21 to the environmental fate data requirements table discuss specific criteria for determining whether data from a biodegradation study, the activated sludge sorption isotherm study, and the activated sludge respiration inhibition test are required for a particular product based on its intended uses.

ii. *Trigger for migration study.* EPA made changes to the trigger for the migration study in the final Residue Chemistry Data Requirements in § 158.2290. In its proposed rule, EPA “triggered” the migration study based on anticipated instances such as theoretical (modeled) estimates yielding a risk of concern. One commenter submitted a suggested residue chemistry data requirements table with a line-item entitled “Nature of residue of surface.” (ACC Comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.10; Appendix I, entitled “Comments on Proposed Data Requirements for Residue Chemistry” p. 7). A different commenter also submitted a

different residue chemistry data requirements table, which also included the same line-item entitled “Nature of residue on surface.” (CSPA Comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0086.2).

The commenters’ suggestion of requiring a nature of the residue study on surfaces provides a more definitive trigger for the migration study. EPA is adding a nature of the residue on surfaces study. As specified in test note 5 to the final Residue Chemistry Data Requirements Table, the results of the nature of the residue on surfaces study will serve as a trigger for determining whether the migration study will need to be performed. EPA considers the commenters’ suggestions to be a valuable addition to the final residue chemistry data requirements table in § 158.2290 that provides more definitive triggers to help define and narrow the instances of higher-tiered testing.

iii. *Changes to data requirements for wood preservatives.* As discussed in Unit VI.B., EPA’s current practice of determining the data required for a wood preservative product is dependent upon where the product is intended to be used (land-only versus land and aquatic). This approach also assumes that diversion does not occur and that wood that is treated for land-only uses does not end up in the water and vice versa. In practice, it is difficult to assure that diversion does not occur. Accordingly, in response to comments, the Agency determined that all treated wood needs to be considered as having the potential to come into contact with surface water. Therefore, for the final Environmental Fate Table, for the wood preservatives column, the data requirements for anaerobic soil metabolism, aerobic aquatic metabolism, and anaerobic aquatic metabolism were changed from “CR” to “R.” For the final Nontarget Organism Table, for the wood preservatives column, the data requirements for chronic toxicity testing with fish (fish early-life stage) and aquatic invertebrate (aquatic invertebrate life-cycle) are being changed from “CR” to “R” to provide chronic data when chronic exposure is expected. With regards to the three acute toxicity tests conducted with the TEP, the “NR” in the wood preservatives column is

changed to “CR.” Additionally, EPA will perform a down-the-drain analysis for every product with an applicable use or exposure scenario, including wood preservatives, that has the potential for waters containing antimicrobials to reach a WWTP. Therefore, to perform this analysis, the Agency is requiring data on the biodegradation of a wood preservative and its potential toxicity to WWTP microorganisms in an activated sludge basin.

iv. *Changes to data requirements for antifoulants.* Antifoulants are released/applied directly to the aquatic environment. These products are often manufactured to be persistent, and because of the continuous release process, some of the active ingredient is likely to be transferred to the bottom of the water column, and then be adsorbed to the sediment. Therefore, EPA is changing, in the final Environmental Fate Data Requirements Table, the “CR” for the aquatic sediment study for the antifoulant paint and coatings column to “R.” With regards to the three acute toxicity tests conducted with the TEP, the “NR” in the antifoulant paint and coatings column is changed to “CR.” Also, to perform a down-the-drain analysis, the Agency is requiring data on the biodegradation of an antifoulant and its potential toxicity to WWTP microorganisms in an activated sludge basin.

v. *Non-dietary ingestion.* EPA proposed to require this post-application exposure study. However, EPA agrees that instead of requiring this study, it is more likely that EPA would model this route and pathway of exposure using inputs from available and reliable published research. Therefore, EPA has removed this data requirement from the final Post-Application Exposure Table.

vi. *Re-structuring of proposed toxicology and residue chemistry data requirement tables.* In the proposed rule, for the toxicology data requirements table, EPA separated those use patterns needing more toxicology data from those needing less toxicology data using a terminology described as high or low. Based on comments received, in this final

rule, EPA is now using a food/nonfood approach with some similarities to that of the toxicology data requirements table for conventional pesticides to distinguish the use patterns that need more toxicity data from those that need less. The food-use column and the nonfood-use column are split into subcolumns to explain which food-uses or nonfood-uses require more data, and which require less. This modification of the food/nonfood approach delineates the specific data requirement needs for antimicrobial pesticides.

For the final residue chemistry data requirements table, EPA has adopted the commenters' suggestion for a tiered format. After review of the commenter's suggested tables, EPA believes the commenters' suggested tiered approach is more suitable to antimicrobials than that proposed by EPA.

vii. *Change in terminology.* The commenters' asserted that the use of terms such as "high" or "low" as a means of tiering was insupportable, and an "unsubstantiated assignment of exposure categories" (ACC Comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.1, p. 21 and 22). EPA continues to believe that the use of "high" and "low" categories of exposure defined by the antimicrobial use patterns are a valid method for identifying those exposures that have greater exposure and those that have less. Based on its experience, EPA understands which use patterns require more data. However, EPA can achieve the same result without the use of the terms "high" or "low." Therefore, based on comments received, EPA notes that it is no longer using the terms "high human exposure" and "low human exposure" as table headers for the final Antimicrobial Toxicology Data Requirements Table. Similarly, EPA is no longer using the terms "high environmental exposure" and "low environmental exposure" as table headers for the final Antimicrobial Nontarget Organism, the Nontarget Plant Protection, or the Environmental Fate Data Requirements Tables. However, EPA also notes that terms such as "high human exposure," "low human exposure," "high environmental exposure" and "low environmental exposure" can be appropriate when discussing a particular

antimicrobial use. A statement that a particular use results in, for example, “high environmental exposure” provides information and alerts the reader that more data are likely to be needed, rather than less data.

IV. Scope of the Rule

This rule establishes a separate listing in Title 40 of the CFR for EPA’s data requirements under FIFRA and FFDCA section 408 for antimicrobial pesticide uses. Although the rule is tailored to the unique characteristics of antimicrobial pesticides, it builds upon the existing data requirements imposed in 1984 on all pesticides and the 2007 amendments to those requirements pertaining to conventional pesticides. Both sets of data requirements – conventional and antimicrobial – are designed to provide EPA with the information needed to make the required regulatory determinations under FIFRA and FFDCA section 408. FIFRA provides that a pesticide may not be registered for sale, distribution, and use unless “it will perform its intended function without unreasonable adverse effects on the environment” [7 U.S.C. 136a(c)(5)(C)]. FIFRA defines “unreasonable adverse effects on the environment” as both “any unreasonable risk to man or the environment” and “a human dietary risk . . . inconsistent with the standard under section 408 of the [FFDCA]” [7 U.S.C. 136(bb)]. FFDCA section 408 directs that EPA shall not establish a tolerance permitting pesticide residues in food unless EPA determines that the tolerance is “safe” [21 U.S.C. 346a(b)(2)(A)(i)]. “Safe,” under FFDCA section 408, is defined as “a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information” [21 U.S.C. 346a(b)(2)(A)(ii)]. In making safety determinations, EPA is required to consider aggregate and cumulative exposures from pesticides and other related substances and multiple factors specifically related to the protection of children [21 U.S.C. 346a(b)(2)(C) and (D)].

Under FIFRA, EPA has required “[s]ubstantial amounts of data on the pesticide, its

composition, toxicity, potential human exposure, environmental properties, and ecological effects, as well as information on its product performance (efficacy) in certain cases” (73 FR 59384, October 8, 2008). Since 1984, EPA has had codified FIFRA data requirements mandating data on, among other things, the toxicity hazards from ingestion of pesticides and exposure levels of pesticide residues in food (Ref. 2). With the passage in 1996 of the Food Quality Protection Act, [Public Law 104-170, 110 Stat. 1489 (1996)], which added the expanded safety standard in FFDCA section 408 described previously, EPA’s data needs have expanded. As noted in the preamble to the proposed rule, “[t]he combination of aggregate and cumulative exposure assessments required by FFDCA section 408 increases the nature and scope of EPA’s risk assessment, and potentially increases the types and amounts of data needed to determine that the FFDCA safety standard is met” (73 FR 59385, October 8, 2008). Moreover, with the explicit linkage in FIFRA between the FIFRA and FFDCA section 408 safety standards (also added by FQPA), “[t]he data required to support a determination of ‘reasonable certainty of no harm’ under FFDCA are an integral part of the data needed for an ‘unreasonable adverse effects’ determination under FIFRA” [Id.; see 72 FR 60934, October 26, 2007 (FRL-8106-5), recodifying part 158 data requirements under the authority of both FIFRA and FFDCA section 408]. This rule, establishing specific data requirements for antimicrobial pesticides, is designed to capture the broad range of data needed to assess the safety of pesticides under the standards of both FIFRA and FFDCA section 408.

The ACC Biocides Panel and other commenters, however, have claimed that the scope of the proposed rule exceeds the EPA’s statutory authority because EPA is asserting “jurisdiction under FIFRA over some antimicrobial food uses where, in the Panel’s view, the statutory scheme provides exclusive jurisdiction to FDA” (Food and Drug Administration). (ACC Comment identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.1, p. 31). Although the ACC Biocides Panel acknowledges that

these uses are properly regulated by EPA as “pesticides” under FIFRA, the Panel argues that “EPA’s responsibility for such use[s] is to evaluate whether the antimicrobial meets the standard for registration under FIFRA, taking into account FDA’s existing regulatory finding [under FFDCA section 409]. . . . EPA does not have the authority under either FIFRA or FFDCA to review or change the terms of the FDA approval.” (ACC Comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.1, p.33). In essence, the Panel is asserting that for these antimicrobial uses, EPA is without authority or jurisdiction under FIFRA to evaluate, or require data on, the level of risk from dietary exposure to the antimicrobial – where FDA has evaluated the safety of the use of the substance under section 409. As a basis for this argument, the ACC Biocides Panel points to the Antimicrobial Regulation Technical Corrections Act (ARTCA), [Public Law 105-324, in 1998], which divided FFDCA jurisdiction between EPA and FDA with respect to antimicrobials. The Panel further argues that EPA is wrong to rely on FIFRA section 2(bb)’s inclusion of the FFDCA section 408 safety standard in the definition of “unreasonable adverse effects” as authority for requiring data on antimicrobial uses falling under FDA’s FFDCA section 409 jurisdiction. Labeling EPA’s interpretation of FIFRA section 2(bb) in the proposed rule as “new,” the ACC Biocides Panel claims that EPA has contradicted its “long-standing” interpretation of this provision.

The ACC Biocides Panel fundamentally misunderstands EPA’s statutory authority under FIFRA to require data pertaining to dietary risk from pesticides. EPA’s authority to regulate pesticides under FIFRA with regard to their dietary risk is derived from FIFRA not the FFDCA. Under FIFRA, EPA is charged with protecting the public from “unreasonable adverse effects on the environment.” As noted previously, FIFRA in section 2(bb) defines “unreasonable adverse effects” in the first instance as “any unreasonable risk to man” [7 U.S.C. 346(bb)]. This broad standard clearly encompasses any unreasonable *dietary* risk. EPA’s authority to regulate pesticides under

FIFRA on the basis of dietary risk is explicitly reinforced by the second part of the unreasonable adverse effects standard which directs EPA to evaluate “human dietary risks” from “pesticides” under the safety standard in FFDCA section 408. [Id.]

Nothing in FIFRA or the FFDCA limits or constrains EPA’s authority or jurisdiction to regulate pesticides based on dietary risk under FIFRA section 2(bb). The FIFRA section 2(bb) standard is independent from the safety standard under FFDCA section 409. Further, any finding by EPA under FIFRA that considers dietary risk would not “change the terms of a FDA approval;” rather, it would simply be a determination as to whether the separate FIFRA regulatory standard had been met. Finally, contrary to the ACC Biocides Panel’s contention, the adjustment by the ARTCA of EPA’s and FDA’s jurisdiction under FFDCA sections 408 and 409 over antimicrobials does not affect EPA’s jurisdiction or authority with regard to dietary risks of pesticides under FIFRA. In fact, as explained further in this unit, not only did the ARTCA not amend FIFRA section 2(bb) but Congress in the ARTCA took the unusual step of expressly disavowing any intent to narrow the scope of EPA’s authority under FIFRA.

The ARTCA was follow-on legislation to the major 1996 FFDCA amendments which, among other things, changed EPA and FDA jurisdiction under FFDCA sections 408 and 409. Prior to 1996, section 408 of the FFDCA, which is administered by EPA, only applied to “pesticide chemicals” that were defined as FIFRA “pesticides” “used in the production, storage, and transportation of raw agricultural commodities” [21 U.S.C. 321(q) (1994)]. FIFRA pesticide residues in food not falling within this provision (i.e., FIFRA pesticides used later in the food production process than the growth of raw agricultural commodities) came under section 409 of the FFDCA as food additives [See 21 U.S.C. 321(s), 348 (1994)]. FDA administers the establishment of food additive regulations under FFDCA section 409. Many antimicrobial pesticides used in conjunction with the manufacturing and processing of foods, at that time, were regulated as food additives. This

division of legislative authority was changed by the FQPA in 1996. The FQPA amended the definition of “pesticide chemical” in the FFDCA to make it co-terminous with the definition of a “pesticide” in FIFRA by deleting the language restricting pesticide chemicals to those pesticides used in the production of raw agricultural commodities. Correspondingly, the FQPA also excluded “pesticide chemicals” from the definition of a “food additive” [Public Law 104-170 sec. 402, 110 Stat. 1489, 1513 (1996)]. This change had the effect for FFDCA purposes of bringing all FIFRA pesticides under FFDCA section 408. Not only did Congress consolidate regulation of all pesticide residues in FFDCA section 408 but it also amended FIFRA to insure that the new safety standard in FFDCA section 408 was part and parcel of the FIFRA registration standard for pesticides resulting in residues in food [7 U.S.C. 136(bb)(2)]. Specifically, in section 2(bb)(2), Congress defined an “unreasonable adverse effect on the environment” under FIFRA as “a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under FFDCA section 408 [21 U.S.C. 346a].”

In 1998 in the ARTCA, Congress modified slightly its FFDCA decision to consolidate all pesticide chemical residues in foods under FFDCA section 408. ARTCA amended the definition of “pesticide chemical” in FFDCA section 201 to exclude certain antimicrobial substances from the coverage of the definition [*See* 21 U.S.C. 321(q)]. More specifically, with certain qualifications, the ARTCA excepted, from the definition of pesticide chemical, substances that are FIFRA pesticides and are “applied for [an antimicrobial] use on food, or the substance is included for such use in water that comes into contact with food, in the preparing, packing, or holding of the food for commercial purposes.” [21 U.S.C. 321(q)(1)(B)(i)]. In addition, ARTCA excepted substances from the definition of pesticide chemical that are food contact substances, as defined in section 409(h)(6) of the FFDCA, based on certain circumstances related to their use. These antimicrobial substances were now no longer considered “pesticide chemicals” under the

FFDCA but fell under the definition of “food additive.” That had the effect of shifting the residues resulting from these antimicrobial substances from FFDCA section 408 to FFDCA section 409 and shifting agency jurisdiction under the FFDCA over the same from EPA to FDA. Importantly, Congress, in ARTCA, did not amend FIFRA to remove these uses of antimicrobial substances from the definition of “pesticide” under FIFRA and left unchanged FIFRA section 2(bb)(2) which mandates that the section 408 safety standard is part of FIFRA’s unreasonable adverse effects standard as to FIFRA “pesticide” residues on food. Thus, EPA retained FIFRA jurisdiction over these antimicrobial substances (because they remained FIFRA “pesticides”) while FDA reacquired FFDCA jurisdiction over them under FFDCA section 409 (because they were removed from the definition of “pesticide chemical”). To make clear its intent on EPA’s FIFRA jurisdiction, the ARTCA included the following express disavowal which was inserted into the FFDCA definition of “pesticide chemical:”

With respect to the definition of the term ‘pesticide’ that is applicable to the Federal Insecticide, Fungicide, and Rodenticide Act, this clause [excluding certain antimicrobial substances from the FFDCA definition of “pesticide chemical”] does not exclude any substance from such definition” [21 U.S.C. 321(q)(1)(B)].

Since its passage, EPA has interpreted the ARTCA according to its plain language, excluding the designated antimicrobial substances from the coverage of FFDCA section 408 but continuing to regulate those antimicrobial substances that qualify as FIFRA “pesticides” under FIFRA and requiring that, when those antimicrobial pesticides result in residues in food, the risks from such residues be consistent with the safety standard in FFDCA section 408. After all, FIFRA section 2(bb)(2), on its face, applies to FIFRA

“pesticides” and not FFDCA “pesticide chemicals.” Any other result would be directly contrary to Congress’ dictate that it was not excluding any substances from the FIFRA definition of “pesticide.” Accordingly, it is well within EPA’s FIFRA authority to require that data be submitted on pesticides to determine if those pesticides meet the FFDCA section 408 safety standard, whether or not those pesticides come within the definition of a FFDCA “pesticide chemical,” so long as the use of those pesticides results in residues in food. On the other hand, the ACC Biocides Panel’s approach would involve amending the language of section 2(bb)(2) in a manner specifically rejected by the Congress when it passed ARTCA.

There is no basis for the ACC Biocide Panel’s claim that EPA’s interpretation of FIFRA section 2(bb)(2) is “new.” The best evidence of the consistent and long-held nature of EPA’s interpretation are the numerous submissions to the Agency from the Panel (and others) over the last 10 years disputing EPA’s plain language approach to FIFRA section 2(bb)(2). (Refs. 3, 4, 5, 6, 7, 8, 9, 10 and 11)

V. Issues Repeated Throughout Most Comments

In evaluating the comments received on proposed part 158, subpart W, EPA noted that four specific comments were routinely repeated throughout most of the entire set of comments. Additional discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Differentiating the Review of Antimicrobials

1. *Comment.* EPA received several comments noting that FIFRA section 3(h)(3)(A)(ii) specifies that EPA must differentiate the review of antimicrobial pesticides from that of other pesticides.

2. *EPA’s response.* FIFRA section 3(h)(3)(A)(ii) specifies, among other things, that, in proposed regulations to accelerate and improve the review of antimicrobial pesticide products, EPA shall define the various classes of antimicrobial use patterns,

differentiate the types of review undertaken for antimicrobial pesticides, conform the degree and type of review to the risks and benefits presented by antimicrobial pesticides, and ensure that the registration process is sufficient to maintain antimicrobial product efficacy. While those elements apply to a proposed rulemaking that the Agency published on September 17, 1999 (64 FR 50671) (FRL-5770-6), the Agency has been mindful of those same elements in its development of part 158, subpart W. As applied to antimicrobial product registration actions, differentiation refers to the tailoring of data requirements so that they are responsive to considerations about the antimicrobial products to which they relate. In practice, differentiation means that the data requirements applied to antimicrobials are designed to respond to the special or unique needs of antimicrobials such as the nature of the products, their ingredients, their uses, etc. Differentiation or tailoring does not mean that the resulting data requirements for antimicrobials will necessarily be comprised of more, less, or the same number and type of data requirements as required for other types of pesticides such as conventional pesticides.

For example, the residue chemistry data requirements for conventional pesticides focus on the application of agricultural pesticides to crops growing in the fields. However, the residue chemistry data requirements for antimicrobials, codified in this final rule, have been tiered to account for applications that focus not on crops growing in the fields (where antimicrobials are rarely used), but instead account for antimicrobial uses, including those that result in residues on food more indirectly, such as from use as sanitizers in food processing plants. The overall impact is to require fewer studies since the tiering used for the antimicrobial residue chemistry data requirements table is structured differently, and there are fewer “R” studies and most studies are “CR.” However, there are two residue chemistry data requirements (migration and nature of the residue on surfaces) for antimicrobials that are not included in the conventional residue chemistry data requirements table because they reflect the unique use sites for antimicrobials; see Unit

XVI. for additional discussion. Ecotoxicity and environmental fate data requirements provide another example of the differentiation of data requirements between antimicrobials and conventional pesticides. While conventional or biochemical/microbial pesticides are often used outdoors, and are deliberately placed/spread in the environment, most antimicrobials are used indoors. As discussed in the preamble (73 FR 59406), previously EPA had assumed that many of the indoor uses went down the drain to a WWTP, where the WWTP processes would mitigate environmental concerns. Therefore, in 1984, EPA required basic ecotoxicity and environmental fate data for conventional pesticides but made these types of data conditional for indoor uses such as antimicrobials based on whether antimicrobial-specific data indicated that environmental exposure may occur. However, as discussed in the proposed rule (73 FR 59407), in recent years there have been detections of antimicrobial chemicals (with indoor uses) in waterbodies. These antimicrobials are moving into the environment via treated effluent. Therefore, EPA is requiring for antimicrobials a specific tiered-set of data to evaluate the likelihood of environmental exposure to antimicrobials that may reach a WWTP, as a result of being washed down the drain via leachates, rinsates, and flushes. These data evaluate whether antimicrobials are likely to survive the treatment processes at a typical WWTP, and thus would be present in the WWTP effluent. Antimicrobials that do survive the treatment processes have the potential to end up in the terrestrial or aquatic environments and higher-tiered ecotoxicity and environmental fate data are only triggered for these antimicrobials.

Thus, differences in data requirements stem directly from the inherent differences in the nature of the particular type of pesticide used. Even with such differentiation or tailoring, there is a general core of data requirements which may be expected to be applicable to any kind of pesticide product, such as product chemistry data requirements. EPA's ultimate goal with its antimicrobial data requirements is to create a body of data requirements which produce sufficient information for the Agency to consider and use in

making its statutorily-required determinations regarding the risks and benefits, where applicable, of antimicrobial pesticides. The differentiation or tailoring of the antimicrobial data requirements is instrumental in accomplishing that goal.

B. Rewrite and Repropose the Rule

Several commenters requested that EPA rewrite and then repropose this rule. Commenters raised three arguments as to why EPA should repropose. First, the proposed regulation does not contain scientifically-based criteria for determining data requirements but instead requires that data requirements be determined in case-by-case consultations in which EPA retains “sole discretion” as to the data required. Second, EPA has not disclosed how it plans to use the proposed data in EPA risk assessments. Third, affected parties cannot properly evaluate the data requirements without final guidelines on how such studies should be conducted. Each of these three arguments are addressed in detail in the following responses.

1. *Comment on scientifically-based criteria.* Several commenters focused on the test notes to the data requirements tables, and claimed that the proposed rule “leaves too many standards and decisions to the sole discretion of EPA, creating uncertainty and, inevitability, inconsistency in regulatory decision making.” Too many determinations, the commenter asserted, are at “EPA’s discretion” because the proposal is vague, without clear-cut criteria. Additionally, they argued that there are too many places in the test notes where consultation with the Agency is required or the phrase “as determined by the Agency” is used. (One commenter listed 37 instances in which the proposal allegedly substituted a mandatory consultation process for regulatory criteria.) According to the commenters, EPA should eliminate most of the consultation requirements and instead, repropose the rule providing a clear set of requirements.

2. *EPA’s response to comment on scientifically-based criteria.* Test notes often contain qualitative or quantitative measures for use in determining whether a study is

triggered or not. Most frequently this occurs when there is an initial study that relates to whether subsequent testing would be needed or not. Not all triggers are easily reduceable to quantitative measures and EPA believes that qualitative descriptors such as “expected to enter the environment in significant concentrations,” or “if repeated dermal exposure is likely to occur under conditions of use,” and “the use of the pesticide is likely to result in repeated human exposure over a considerable portion of the human lifespan” provide meaningful criteria for determining when a study is triggered. EPA has carefully reviewed each of the 37 test notes cited by one commenter and has identified several instances in which clarification of the criteria was appropriate. EPA’s analysis of these 37 test notes and resultant changes are included in response to comment 3 in the Response to Comments Document in the docket.

In numerous places the test notes contain language stating that the criteria would be applied “as determined by the Agency.” Commenters have misinterpreted this as giving EPA the authority to make decisions on factors other than the regulatory criteria included or in its “sole discretion.” This was not EPA’s intent and, accordingly, EPA has removed all of the phrases “as determined by the Agency” from all test notes for the final antimicrobials rule so there can be no chance of a misunderstanding of how the criteria are to be applied.

Commenters also asserted that the EPA’s alleged mandatory consultation requirements rendered the test notes meaningless, as EPA would determine whether studies were required in private based on unspecified factors. EPA disagrees. The commenters have misread the proposed rule language and misunderstood the purpose for consultation. The consultation references were not intended to impose a mandatory consultation requirement. To the contrary, references to consultation were an attempt by EPA to signal its willingness to meet with applicants to adapt studies, if necessary, to the specifics of individual antimicrobials.

Consultation is a longstanding, commonly used and valuable process in EPA's Pesticide Program. Applicants often meet with OPP staff on a pre-submission basis to review and discuss the adequacy of the available data. OPP believes that such meetings are beneficial to both EPA and the applicants. In practice, such meetings are very often sought by registrants and applicants. By encouraging communication and exchange of ideas, such discussions can help in the development of clearer expectations of what must be submitted in instances where data requirements involve complexities. Consultation can result in data that better meets EPA's needs and saves resources for both EPA and the applicant. Depending upon what is intended to be addressed, such meetings do not necessarily need to be held in person, but can be frequently accomplished via teleconferencing.

EPA did not intend its references to consultations in the test notes to impose mandatory consultation requirements; neither did EPA intend the consultation references as a means of establishing a different standard for determining if a study is triggered. EPA has carefully reviewed all test notes in the antimicrobials final rule and removed all references to consultation from all test notes for the antimicrobials rule so there can be no chance of misunderstanding the voluntary nature of consultation.

3. *Comment on use of data in risk assessment.* The commenters also argued that reproposal was necessary because they could not meaningfully comment on the proposal without understanding how the data would be used by EPA. Specifically, one commenter wrote: "It is not plausible for [the commenter] or others to meaningfully comment on the Proposal without the benefit of understanding the risk assessment approaches EPA plans to use, (e.g., human and ecological), the ways in which the data requirements will provide information to conduct those assessments and the ways EPA will use those risk assessments in making regulatory decisions."

4. *EPA's response on use of data in risk assessment.* EPA disagrees with this

comment for several reasons. First, how EPA conducts risk assessments and how it uses toxicological, ecological, and exposure data in those risk assessments is well known. Risk assessment is not unique to OPP. The principles used by OPP and, in fact, by EPA are those used by the scientific community in general. OPP follows the processes and procedures in the many risk assessment guidance documents that have been issued by EPA (see <http://www.epa.gov/riskassessment/guidance.htm>). The Agency's exposure and risk assessment procedures have been presented in numerous exposure and risk assessments for antimicrobial pesticides. EPA's assessments reflect the best available data, and the state of the science of exposure and risk assessment models, methods, and procedures.

Moreover, OPP's risk assessment procedures for pesticides are well-documented. EPA has concluded the process of completing Reregistration Eligibility Decision Documents for all pesticides under FIFRA and reassessing all FFDCA pesticide tolerances. This was a very open process involving multiple public comment opportunities as to each pesticide. Further, all regulatory decision documents as well as the underlying risk assessments have been made available to the public. EPA has now begun new pesticide reviews under the Registration Review program, and that process is equally open and transparent.

A second reason why EPA believes this comment to be misdirected is that the proposed rule does not represent a change to EPA's existing and transparent risk assessment procedures. Rather, the proposal is merely designed to tailor the existing data requirements that apply to all pesticides in a way that is more specific to antimicrobial pesticides, as well as including some new requirements applicable to antimicrobials.

Finally, the comment is without foundation because EPA has explained the need for each study and provided background information on the purpose for which each study would be required. Part 158, subpart B contains an extensive description of the need for and use of submitted studies (40 CFR 158.130). Additionally, as explained in the

preamble to the antimicrobials proposed rule, EPA relied on the proposed and final rules for establishing data requirements for conventional pesticides. As stated in the proposed rule for antimicrobials, the rationales for requiring and/or revising particular data requirements were in those rules.

With few exceptions, these rationales are also applicable to antimicrobial pesticide chemicals, and as such have not been repeated in today's proposed rule. Today's proposal discusses in detail only those revisions that are singularly applicable to antimicrobial pesticides, including antifoulants and wood preservatives." (73 FR 59384).

Examples of studies applicable to antimicrobial pesticides and for which a description of the need for the requirement was included in the preamble to the proposed rule for antimicrobials include the need for:

- The 90-day dermal and 90-day inhalation studies for heating, ventilation, air conditioning, and refrigeration uses (73 FR 59395),
- A food migration study (73 FR 59404), and
- Environmental fate studies to support a down-the-drain assessment (73 FR 59408).

One commenter presented several examples of what the commenter labeled as EPA's "ad hoc risk assessment processes." An examination of those examples shows that the commenter is concerned with what it labels as "inconsistency in EPA's current practice" as to when a dietary risk assessment is needed for antimicrobial pesticides. The commenter argued that this alleged inconsistent practice shows the "need for stable, transparent guidance on risk assessment to support data requirements regulation." EPA

does not believe that it has been inconsistent in its risk assessments. Furthermore, EPA does not believe that such “inconsistencies,” if they exist, would mean that affected parties could not comment meaningfully on the proposed data requirements. Ultimately, the issue with the data requirements rule is whether EPA has asked for data needed for determining whether pesticides meet the relevant statutory safety standards. The fact that EPA might have been inconsistent in the past in its determinations with regard to the safety standard or how it went about assessing whether a pesticide met the safety standards (e.g., did EPA need to do a dietary risk assessment), does not handicap an affected party in determining whether a proposed data requirement is consistent with the statutory safety standards. To reiterate, the relevant question is not whether EPA has guidance on when dietary risk assessment is needed but whether the proposed data requirements pertaining to dietary risk would require information that are appropriate to EPA’s determination under the applicable statutory safety standards. To the extent, the commenter is concerned with any particular Agency decision regarding when a dietary risk assessment is needed for antimicrobials, EPA encourages the commenter to raise that concern directly with the Agency in the context of the specific matter causing the commenter concern.

This commenter later filed additional comments that further developed the argument that reproposal is necessary because EPA allegedly has not clearly defined when a dietary risk assessment is needed. The commenter wrote: “[T]he Proposal does not clearly articulate any standards for determining what uses trigger a food analysis. It has become apparent since the Proposal was issued that the Agency will interpret this regulation to vastly increase the number of antimicrobials regulated as food use.”

(ACC/CSPA letter, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0107, p. 2). Further, the commenter then asserts that “EPA’s economic analysis does not even attempt to address the increase in the burden on registrants and applicants that this [alleged] expansion of the need for ‘food contact’ approvals will cause.” (Id.) These

additional comments suggest that this commenter is concerned with EPA decisions issued prior to this final rule (and, in most cases, prior to issuance of the proposed rule) and fears how the final rule may be interpreted in the future. However, it is difficult to determine from these comments whether the commenter is claiming that this alleged “expansion” of food use antimicrobials is effected by any particular language in the proposed rule. To the extent the commenter is arguing that the expansion is caused by EPA’s application of the FFDCA section 408 standard to all antimicrobial food uses under FIFRA section 2(bb) (whether the use requires clearance under FFDCA section 408 or 409), the commenter, as explained in Unit XVI.A., misunderstands EPA’s authority under FIFRA and EPA’s practice as to antimicrobials since the passage of ARTCA. In another place in its subsequent comments, the commenter argues that the use of the categories of “direct food use” and “indirect food use” “creates the potential for almost all antimicrobials to be considered as possibly leaving residues on food.” (ACC attachment 1, identified in the docket by document ID number EPA-HQ-OPP.2008-0110-0108, p. 4). However, EPA adopted the categories of direct and indirect food use as a way to tier data requirements for residue chemistry and toxicology, not to expand the category of food uses. For a use to qualify as an indirect food use it must result in residues in food and EPA clearly has the authority under FIFRA and the FFDCA to request data on and assess the risk of pesticide residues in food. Despite the commenter’s claims to the contrary, it is not EPA’s intent to use this data requirements rule as a basis for expanding what antimicrobial uses qualify as direct or indirect food uses. Accordingly, EPA’s economic analysis has accurately captured the costs imposed by this rule.

5. *Comment on lack of final guidelines.* Finally, commenters argued that reproposal was needed because affected parties cannot properly evaluate the data requirements without final guidelines on how such studies should be conducted.

6. *EPA’s response on lack of final guidelines.* EPA disagrees with this comment:

EPA can require submission of a particular study even if no guideline has been provided. The types of data needed for EPA to make a registration decision are clearly identified in its proposed rule. Testing laboratories routinely conduct these studies, as evidenced by the test cost data which was available for use in both EPA's and the commenter's economic analyses. Final guidelines are available for the majority of tests required, and draft guidelines provide information for the applicant to consider. Since there was an understanding of the types of data EPA proposed to require, the commenter had sufficient information to comment on whether EPA had asked for the data needed for determining whether pesticides meet the relevant statutory safety standards.

It is important to keep in mind that, as noted in the proposed rule, new part 158, subpart W is "retaining most current data requirements for antimicrobials. . . and revises other existing data requirements." (73 FR 59383) The guidelines that the commenter asserts as not providing sufficient information to permit meaningful comment pertain, for the most part, to these existing data requirements that are not being modified by this rulemaking. As to the "new" data requirements that are imposed by this rule, the commenter has not specifically explained why interested parties cannot meaningfully comment on these requirements or why a final guideline is needed to provide meaningful comments on these studies. In fact, as to these "new" studies, OCSPP guidelines (formerly OPPTS) are available for all except the nature of the residue on surfaces study. For that study, due to the many site- and chemical-specific variations, a protocol review is required.

This commenter later filed additional comments stating that "FIFRA requires EPA to issue test guidelines." (ACC/CSPA letter, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0107, p. 4). In accordance with FIFRA section 3(c)(2)(A), EPA has promulgated data requirement rules "specifying the kinds of information which will be required to support the registration of a pesticide." EPA is not required to issue guidance explaining how studies that are addressing the data required

under the regulations should be performed. Additional information on EPA's development of guidelines is in Unit XVIII.

C. Alternative Testing Paradigms.

1. *Comment.* A commenter asked how OPP plans to implement the National Academy of Sciences (NAS)/EPA Vision of Toxicity Testing in the 21st Century or the Strategic Plan for Evaluating the Toxicity of Chemicals. The commenter noted that the rule should be specific in identifying alternative approaches that EPA will consider.

2. *EPA's response.* In the proposed rule, in Unit XVIII., entitled "Alternative Testing Paradigms," EPA discussed its commitment to moving towards a more efficient and refined testing/risk assessment paradigm for antimicrobial pesticide chemicals. That discussion included the following:

- OPP's current thinking on how Structure-Activity-Relationships (SAR) and Quantitative SAR (QSAR or (Q)SAR) modeling could be used as part of an integrated approach to hazard and risk assessment to support a regulatory decision-making process for antimicrobial pesticides.
- The evolution of the current paradigm of animal (*in vivo*) toxicity testing toward a more integrated tiered testing approach for antimicrobial pesticides.
- Development of computational tools for interpreting data from computational chemistry, high-throughput screening (HTS) and genomic technologies.
- The EPA-funded reports by the NAS entitled "Toxicity Testing for Assessment of Environmental Agents" (2006) and "Toxicity Testing in the 21st Century: A Vision and a Strategy" (2007).

The NAS recommendations are truly visionary and involve a transformative paradigm shift in toxicology based largely on the increased use of *in vitro* molecular and cellular assays, and computational modeling that make testing faster and less costly, and

reduces animal testing significantly. The new technologies are expected to help EPA better understand how chemicals perturb normal biological function(s), and thus identify toxicity pathways. Potential toxic effects of chemicals could then be predicted based on *in vitro* bioactivity profiles derived from a chemical's effects on cellular molecules and processes. Thus, the scientific foundation for this new paradigm is based on linking *in vitro* effects with adverse outcomes *in vivo*, and on computer modeling that extrapolates to predicted responses in whole tissues, organisms and populations based on realistic human or environmental exposures.

EPA is working to develop and evaluate new technologies in molecular, cellular, and computational sciences to supplement or replace the more traditional methods of toxicity testing and risk assessment (see <http://www.epa.gov/pesticides/science/testing-assessment.html>). Such an approach begins with consideration of exposure information along with hazard-based hypotheses about the plausible toxicological potential of a chemical or group of chemicals based on their physical-chemical properties and their effects on biological targets *in vitro*. This information is then combined with computer modeling to target animal testing to the specific data needed for human health and ecological risk assessments.

No single new technology will be able to address all situations. However, by using a suite of tools and approaches in combination, EPA believes it is possible to improve the hazard and exposure assessments that form the basis for understanding pesticide chemical risks. It will take time and substantial research to build this new approach. OPP will incorporate the new technologies into EPA's hazard and risk assessment processes as the technologies are sufficiently developed and peer reviewed. Development and vetting of this new approach to chemical management must be accomplished while continuing to make pesticide registration decisions. Eventually, the new technologies should:

- Create a broader suite of computer-aided methods to better predict potential hazards and exposures, and to focus testing on likely risks of concern.

- Improve the approaches to more traditional toxicity tests to minimize the number of animals used while expanding the amount of information obtained.

- Improve OPP's understanding of toxicity pathways to allow development of non-animal tests that better predict how exposures relate to adverse effects.

- Improve the diagnostic biomonitoring and surveillance methods to detect chemical exposures and identify causes of toxic effects.

Since the publication of the proposed rule in October 2008, OPP announced its strategic direction to move toward an improved testing and assessment paradigm where *in vivo* (animal) testing would be targeted to the most likely hazards of concern. OPP envisions an enhanced testing/assessment paradigm that is a progressive, tiered-testing approach. This paradigm shift should accrue the following benefits to OPP:

- Ability to evaluate more chemicals across a broader range of potential effects in a shorter time frame.

- Potential to increase the feasibility of assessing the risks posed by mixtures.

- Enhanced predictive ability to determine whether animal testing is needed to refine a risk assessment and to inform management decisions.

- Refine and reduce animal testing by maximizing information obtained from animal studies, and focusing on effects of concern.

- Opportunities for improved diagnostic biomonitoring and surveillance methods to detect chemical exposures and identify causes of toxic effects.

- Enhance the quality and efficiency of risk assessment and risk management decisions.

Over the next several years, OPP intends to improve and transform its approach to

pesticide risk management by enhancing its ability to use integrated approaches to testing and assessment. The Agency's work on an integrated approach means the development of increasingly effective laboratory animal tests that are designed to maximize the information generated about the nature of the effects being studied. OPP intends to expand its toolbox of predictive models. The new toxicity and exposure approaches will enhance priority-setting and screening approaches and therefore focus Agency and societal resources on those chemicals with the greatest risk potential.

These advances will be incorporated within a risk assessment framework of problem formulation, hazard, dose response, exposure assessment, and risk characterization to support pesticide registration decisions. As this framework evolves, EPA will create pilot programs and develop guidance documents to inform applicants and others of the alternative approaches being used.

It will require many years to realize the NAS vision of a new toxicity paradigm based on evaluating perturbations in cellular pathways by reliance on an array of computational and *in vitro* methods. However, the development and expansion of certain tools used to guide more intelligent *in vivo* testing is anticipated to become available in the nearer term (≤ 5 years) which includes (Q)SAR/expert systems, TTCs, and *in vitro* technologies. As EPA transitions to the use of these components of intelligent testing or alternative methods, communication will be essential. Through its Pesticide Program Dialog Committee, OPP has created a 21st Century Toxicology/New Integrated Testing Strategies Workgroup. For information, see <http://www.epa.gov/pesticides/ppdc/testing/index.html>.

Additionally, OPP has and will continue to publicly vet this new approach. On May 24 – 26, 2011, OPP requested that the FIFRA SAP consider and revise a set of scientific issues related to Integrated Approaches to Testing and Assessment (IATA) Strategies: Use of new computational and molecular tools. OPP plans to build on an

established foundation of using a variety of tools in a tiered testing and assessment framework by systematically adding new tools and methodologies, as well as an advancing understanding of key events in toxicity pathways. OPP requested the SAP's input on EPA's plans to maximize use of existing data from similar compounds, including information from new toxicity hazard computational and *in vitro* predictive models, and exposure modeling to target *in vivo* toxicity testing that is necessary to assess and manage chemical risks, appropriately. Two case studies illustrated the use of these approaches. The SAP Report is available at

<http://www.epa.gov/scipoly/sap/meetings/2011/052411meeting.html#frn>.

VI. Antimicrobial Use Patterns

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Definitions of Use Patterns

1. *Comment.* The commenter suggested different use patterns for EPA to consider. The commenter believes that the use patterns proposed by EPA are not use patterns but descriptions of product types. The commenter suggested six general use patterns for EPA to consider. These include:

- Indoor industrial (all nonfood);
- Indoor residential/commercial/institutional nonfood;
- Indoor commercial/institutional food;
- Aquatic areas nonfood;
- Aquatic areas food;
- Material preservative for exempt treated article uses.

2. *EPA's response.* The Agency disagrees that these suggested use patterns are

adequate substitutes for the proposed use patterns. The use patterns that EPA proposed provide a reasonable approach for allowing the Agency to more clearly identify and tailor the data requirements for the different types of antimicrobial pesticides. In some cases, that is best accomplished by using the product type to define the use pattern.

EPA has reviewed the commenters' descriptions of their six suggested general use patterns and has determined that they do not acknowledge all potential exposure pathways of antimicrobial pesticides, particularly those discharged to wastewater as a result of processing and end-use. Although three of the proposed general use patterns include "indoor" in the name, the exposure potential for these use patterns is not limited to the indoor environment. This is because these patterns include processes and end-uses of antimicrobial pesticides that are discharged to wastewater, thereby leading to the potential for microorganisms in WWTPs to be exposed to antimicrobial pesticides and for aquatic organisms to be exposed to antimicrobial pesticides in surface water downstream of WWTPs. If the antimicrobial is not completely removed during treatment, exposures of humans to antimicrobials may also be associated with antimicrobials discharged to wastewater that enters WWTPs and subsequently enters surface water via WWTP effluents. Furthermore, there may also be the potential for terrestrial organisms and humans to be exposed to antimicrobial pesticides if the antimicrobial that is discharged to wastewater partitions to biosolids.

Since the processing or end-use of an antimicrobial pesticide in an indoor setting does not preclude the potential for its release to ambient environmental media, particularly under circumstances in which there is potential for discharges of antimicrobial pesticides to wastewater, EPA believes that the designation of an antimicrobial use pattern as "indoor" is misleading. Based on the conclusion that processing or end-use of an antimicrobial pesticide in an indoor setting does not preclude its release to the ambient environment, EPA believes that a down-the-drain analysis is needed for all use patterns with the

exception of the aquatic areas use pattern.

The commenter's suggested use patterns are also inconsistent with EPA's reevaluation of the data required for wood preservatives. In response to comments, the Agency determined that all treated wood needs to be considered as having the potential to come into contact with surface water. Therefore, for wood preservatives, EPA has changed several data requirements in both the environmental fate table and the non-target organisms table from "CR" to "R." However, under the commenter's six suggested use patterns, wood preservatives would be considered to be the same as material preservatives. The commenter did not differentiate the data needed between the two use patterns. EPA believes that the data needed for a wood preservative is distinctly different from that needed for a materials preservative. Wood preservatives have a high potential for environmental exposure, as evidenced by both environmental fate and nontarget organisms data requirements that are "R." Material preservatives have a lower potential for environmental exposure and consequently are "CR." Thus, the data requirements codified in this final rule acknowledge the differences in the data needed by having two distinctly different use patterns: Wood preservatives and material preservatives.

Given the inclusion of the term "indoor" as part of the title of three of the suggested use patterns, and the combining of wood preservatives and materials preservatives into a single use pattern, EPA believes that the six general use patterns suggested by the commenter would not adequately serve EPA's or the public's needs. Additionally, the 1997 review by the FIFRA SAP of EPA's 12 antimicrobial use patterns indicated the SAP's agreement that the Agency's proposed designation of 12 use patterns was a reasonable approach to organizing data requirements, and was, in fact, similar to the approaches used by Canada's Pest Management Regulatory Agency (PMRA), and the California Environmental Protection Agency. Therefore, EPA is codifying the 12 use patterns that were proposed.

B. Wood Preservative Use Pattern

1. *Comment.* Several commenters questioned how wood preservatives were treated in the proposed rule. One commenter thought that all wood preservatives should be considered as having contact with water. Another commenter argued that the industrial, commercial and do-it-yourself uses of wood preservatives are different and should be assessed differently.

2. *EPA's response.* Wood preservatives are pesticides for incorporation into wood products to control wood degradation problems due to fungal rot or decay, sapstain, molds, or wood-destroying insects.

As explained in the proposed rule, (73 FR 59405) EPA's current practice of determining the data required for a wood preservative product is dependent upon where the product is intended to be used (land-only versus land and aquatic). Under this approach, fewer environmental fate and ecological effects studies are required for products that limit their use patterns to land-only uses. This approach also assumes that diversion does not occur and that wood that is treated for land-only uses does not end up in the water and vice versa. EPA specifically requested comments on the regulation of wood preservative products, and indicated that based on the comments received could determine to continue with the current practice of considering land-only applications, or change to a land and aquatic usage. Based on comments indicating that the data required to register a wood preservative should not differentiate between land only and aquatic only applications of treated wood, EPA has reevaluated this approach. As discussed in the proposed rule, it is difficult to assure that diversion does not occur. EPA considered three possibilities:

- Assume all treated wood could have the potential to come into contact with surface water.
- Use an approach similar to that advocated by the American Wood Protection

Association (AWPA) approach which differentiates between marine/freshwater and ground contact use/above ground contact use.

- Maintain status-quo.

Wood preservatives used to protect wood structures placed directly in or over water (e.g., marine pilings, docks) will leach active ingredient into the water, resulting in potential exposure of aquatic organisms. Wood preservatives used in the terrestrial environment for uses such as fences, siding, and decks will leach active ingredient into soil where it may be transported into the aquatic environment and expose aquatic organisms.

The Emission Scenario Document (ESD) for Wood Preservatives prepared by the Organisation for Economic Co-operation and Development (OECD) as part of its Series on Emissions Scenario Documents provides guidance on how to estimate emissions of chemical substances in wood preservative products to air, water, and soil as a result both of product application and storage of treated wood prior to shipment and treated wood-in-service. This OECD ESD documents the occurrence of pathways of release of chemical substances during wood preservative application to facility drains that subsequently convey wastewater to WWTPs; entry of chemical substances to adjacent surface water bodies by way of run-off water from unpaved storage of wood preservative-treated products following a rain event; and leaching of chemical substances from in-service uses of treated exterior wood out of ground (i.e., fences, noise barriers), wood in-ground (transmission poles, fence posts), and wood in direct contact with fresh and sea water (poles and planks/decking of jetties and wharfs). Additional information on indirect releases to surface water of antimicrobial pesticides used as wood preservatives can be found in response to comment 134.1 in the Response to Comments Document in the docket.

Given the number of pathways identified that result in potential exposure from

treated wood, the Agency determined that all treated wood should be considered as having the potential to come into contact with surface water. All wood preservative risk assessments will now be performed considering that the treated wood could end-up either on the land or in the aquatic environment. As previously discussed, there are multiple pathways for wood preservative degradates and/or leachates to reach surface water. The AWWA approach would have continued the practice of determining the data requirements based on the intended use site of the treated product.

Given this decision, that all treated wood could have the potential to come into contact with surface water, the wood preservative columns of the final Environmental Fate and the Nontarget Organisms Tables were revised.

For the final Environmental Fate Table, for the wood preservatives column, the data requirements for anaerobic soil metabolism, aerobic aquatic metabolism, and anaerobic aquatic metabolism were changed from “CR” to “R.” Because treated wood products have outdoor usages, the Agency believes that these products have the potential to come into contact with surface water as well as soils which can become flooded or waterlogged and then be released to surface water.

For the final Nontarget Organism Table, for the wood preservatives column, the data requirements for chronic toxicity testing with fish (fish early-life stage) and aquatic invertebrate (aquatic invertebrate life-cycle) are being changed from “CR” to “R” to provide chronic data when chronic exposure is expected.

The Agency agrees that the industrial, commercial, and do-it-yourself uses of wood preservatives are different in terms of human exposure. Industrial wood preservative uses are assessed for those workers involved in the actual treatment of the wood with the preservative. This includes operations at a pressure treatment facility where workers add the preservative to treatment cylinders, remove treated wood charges from the cylinders, check the treated wood to verify retention rates, and move the freshly treated wood around

the facility (from cylinder to drip pad to storage to shipping). Industrial sapstain wood preservatives are also assessed at the treatment facility for the application of the pesticide. Worker tasks for the non-pressure treatment (non-PT) are slightly different than those at pressure treatment (PT) facilities. Separate exposure measurements unique to each type of treatment (PT vs non-PT) are used in the assessments.

Exposures to commercial and do-it-yourself uses of treated wood are assessed for those installing the treated wood and for those exposed to the treated structures (e.g., play sets and decks).

VII. General and Administrative Issues

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Scientific Advisory Panel (SAP) Waivers

1. *Comment.* A commenter noted that in the preamble to proposed part 158, subpart W, EPA cites multiple SAP reports that did not specifically mention antimicrobial pesticides. Therefore, the commenter believes these SAP reviews were insufficient.

Another commenter noted that it has been 9 years since the last SAP review and that EPA should request another SAP review prior to implementation of proposed part 158, subpart W. Still another commenter believes that EPA's request that the SAP waive its review of proposed part 158, subpart W based on the SAP's 1997 review was improper, and that the SAP cannot waive its statutory review obligation.

2. *EPA's response.* EPA disagrees with the comments. On June 3, 1997, EPA presented an early version of the part 158, subpart W proposal in an open meeting to the SAP. At that time, the SAP provided extensive comments in five areas: Toxicology, residue chemistry, ecological effects and environmental fate, human exposure, and efficacy. Since then, the SAP has considered many specific studies and scientific issues

included in proposed part 158, subpart W as part of their reviews of guidelines and of data requirements for conventional agricultural pesticides (see the documents identified in the docket by document ID numbers EPA-HQ-OPP-2008-0110-0032, -0033, -0034, -0035, and -0036). In 1997, the SAP also noted its concern about the possible effects of antimicrobials on WWTPs. Partially in response to the SAP comments, EPA proposed a tiered set of environmental fate data requirements that will allow the Agency to better characterize potential incidences of antimicrobials in surface waters, as a result of down-the-drain uses of antimicrobials.

When the Agency prepared to propose 40 CFR part 158, subpart W, EPA requested that the SAP waive its review of the about-to-be-proposed part 158, subpart W because there were no new scientific issues. The SAP waived its review of the about-to-be proposed part 158, subpart W on February 19, 2008. The Agency continues to believe that there are no new scientific issues that warrant additional review by the SAP. EPA's request for a SAP waiver for the final antimicrobial data requirements rule is discussed in Unit XXIV. FIFRA section 25 requires EPA to give the SAP at least 60 days to review proposed regulations and 30 days to review final regulations. However, the SAP can determine to waive its review during the statutory time periods.

B. Risk Assessments for Wood Preservatives

1. *Comment.* A commenter noted that Canada's PMRA and USEPA conduct risk assessment for wood preservatives differently. EPA's risk assessment is based on the treated wood when used at the final use site, while the PMRA's risk assessment is based at the site where the wood is treated. The PMRA also does not distinguish between terrestrial-only or aquatic-only use for anti-sapstains and heavy-duty wood preservatives.

2. *EPA's response.* The Agency acknowledges differences between its risk assessment of wood preservatives and that of Canada's PMRA. As previously discussed in Unit VI.A. and B., EPA has reevaluated its approach for determining the data required for

a wood preservative product. As part of the reevaluation, EPA considered the human and ecological risks based on exposure pathways identified in OECD's ESD for Wood Preservatives. This ESD identifies potential human and ecological exposures from both treatment of wood at processing facilities and in-service uses on land and in water. The Agency determined that all treated wood should be considered as having the potential to come into contact with surface water. This determination reflects EPA's concern about the potential for the indirect release to surface waters of wood preservatives. As a result, EPA is changing its approach to requiring environmental and ecological effects studies for wood preservatives. All wood preservative risk assessments will now be performed considering that the treated wood could end-up either on the land or in the aquatic environment, thus increasing harmonization between PMRA and EPA with regard to wood preservatives.

C. Clarity on How and When CR Data is Required

1. *Comment.* A commenter asked EPA to specify criteria to determine whether a data requirement is "R" (Required) or "CR" (Conditionally Required). According to the commenter, the discussion of "R" and "CR" suggests that a data requirement labeled "CR" may not be required to be addressed by the applicant. A second commenter stated that it is unclear how and when conditionally required data are triggered. Another commenter asserted that data requirements should be waived only under extraordinary circumstances, and that the use of waivers can effectively preclude appropriate regulation of the pesticide under FIFRA.

2. *EPA's response.* In its proposed data requirement tables, EPA specified whether a data requirement is "Required", "Conditionally Required", or "Not Required" based on how likely the study is needed to complete an assessment of an antimicrobial pesticide. As a rule of thumb, a "Required" study is likely to be needed 50 percent of the time or more and a "Conditionally Required" study is likely to be needed less than 50 percent of the time. Typically, a "Conditionally Required" study is triggered based on the results of a

study that has already been conducted. Triggers in the test notes indicate the circumstances under which the Agency has learned through experience that the information is needed. In many instances, the applicant would be able to make the determination that the trigger has been met and should include the data in their original submission. In other cases, EPA will make the determination based on its review of submitted data and would then request additional data from the applicant. EPA encourages applicants to consult with the Agency to determine the actual need for the data.

All data requirements must be addressed by the applicant by either conducting the study or submitting information that could fulfill the data requirement, such as citing open literature or other data sources, or by requesting and receiving a data waiver. EPA grants data waiver requests only on a case-by-case basis and only when the available evidence indicates a particular study is not needed or that there are particular reasons for not conducting the study. For example, if the physical/chemical properties of the chemical did not lend themselves to the testing procedure, such as performing an inhalation study with a chemical that is a solid and has an extremely low vapor pressure, then a waiver might be granted. EPA also grants waivers in exceptional circumstances, for instance, if a test substance is so corrosive that animal studies would cause undue pain and suffering.

VIII. Product Chemistry

The following represent the significant comments received on the need for and evaluation of product chemistry studies as proposed by EPA. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Application of Subpart D Product Chemistry Data Requirements to Antimicrobials

1. *Comment.* A commenter requested that EPA provide adequate justification for applying the existing product chemistry data requirements for conventional pesticides to antimicrobials without consideration of the highly dissimilar chemistries and inapplicability of many of the requirements.

2. *EPA's response.* It has been EPA's longstanding practice to require product chemistry data. Product chemistry data are required to identify the chemicals used to manufacture a product and to understand the physical and chemical properties of the ingredient or product. Such information is generally independent of the intended use pattern. Product chemistry data are used during label development to identify information to be included on the label, such as the flammability statement, and directions for disposal of the product. Hence, despite any differences between conventional and antimicrobial pesticides, the Agency believes it is appropriate to apply the same product chemistry data requirements to antimicrobials as required for conventional pesticides. The guidelines for conducting product chemistry studies offer flexibility to account for differences between chemical classes.

B. Lack of Adequate Opportunity for Review of Product Chemistry Data Requirements

1. *Comment.* One commenter asserted that registrants of antimicrobial pesticides were not given the opportunity to review and comment on conventional pesticide data requirements that are now being proposed for antimicrobial pesticides.

2. *EPA's response.* In the preamble to proposed part 158, subpart W, EPA proposed to apply the product chemistry data requirements for conventionals in 40 CFR part 158 subpart D to antimicrobial pesticides. Therefore, during the public comment period for proposed part 158, subpart W, from October 8, 2008, to April 6, 2009, any interested party could have commented on the product chemistry data requirements in subpart D (which have been in place since October 2007) and their potential applicability to antimicrobials.

IX. Product Performance Data Requirements

The following represent the significant comments received on the need for and evaluation of product performance studies as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found

in the Response to Comments Document available in the docket to this rule.

A. Product Performance Guidelines

1. *Comment.* Several commenters shared their belief that EPA was seeking to avoid comment on the product performance data requirements in the proposed rule by stating that the Agency “is not proposing to revise product performance data requirements” at this time. Another commenter asked how the product performance section of the proposed rule could be finalized without the 810 guidelines?

2. *EPA’s response.* The proposed product performance data requirements table referenced the older 91 series guidelines. As stated in the proposed rule, the requirements being proposed were “nearly identical” to the existing data requirements in § 158.400 and 161.640, and the table was “transferred essentially unchanged” (73 FR 59391). Since the 2008 proposed rule, EPA published four of the 810 series guidelines (810.2000, 810.2100, 810.2200, and 810.2300 for sterilants, disinfectants and sanitizers) for comment in the **Federal Register** of January 27, 2010 (75 FR 4380) (FRL-8437-2), indicating that these guidelines would be incorporated into the final rule for antimicrobial data requirements. Three additional product performance guidelines (810.2400, 810.2500, and 810.2600) were published for public comment on September 15, 2011 (76 FR 57031) (FRL-8879-1). Thus, in addition to commenting on the draft guidelines themselves, commenters had an opportunity to comment on the inclusion of the 810 series in the Product Performance Data Requirements table.

The availability of the final guidelines for sterilants, disinfectants and sanitizers (810.2000, 810.2100, 810.2200, and 810.2300) was announced in the **Federal Register** of March 16, 2012 (77 FR 15750) (FRL-9332-4), and for the three additional product performance guidelines (810.2400, 810.2500, and 810.2600) in the **Federal Register** of June 27, 2012 (77 FR 38280) (FRL-9349-5).

In this final rule, EPA is replacing the 91 series designations proposed in the part

158, subpart W product performance table with the appropriate 810 series guideline numbers and names. The 810 series guidelines represent the Agency's current recommendations for conducting product performance studies to support antimicrobial pesticide label claims. See Unit XVIII. for a discussion on guidelines.

B. Emerging Pathogens

1. *Comment.* A commenter asked why there is no formal regulatory practice for registering products to address public health emergencies or emerging pathogens promptly and effectively?

2. *EPA's response.* EPA does not believe that the promulgation of a rule dealing with data requirements is the appropriate place to address emerging pathogens. A major consideration in the Agency's process for addressing public health emergencies and emerging pathogens is to work closely with the Centers for Disease Control and Prevention (CDC), USDA, and FDA, as appropriate, to provide a timely and accurate response to these situations. Under FIFRA section 18, the Agency also has authority to grant certain exemptions from the provisions of FIFRA and also to approve the use of unregistered pesticides when emergency conditions exist. Additionally, in April 2008, the Agency implemented a disinfection hierarchy policy for addressing emerging viral pathogens. Information on this policy is available on the EPA website at http://www.epa.gov/oppad001/disinfection_hier.htm. EPA believes that emerging pathogens require flexibility and speed in disseminating information and seeks to address such situations in a prompt and effective manner.

C. Definitions of Sanitizer and Disinfectant

1. *Comment.* Several commenters claimed that the proposed definitions do not reflect the work done by the regulated community in cooperation with EPA since 1999. In particular, these commenters did not agree with the proposed definitions of sanitizer and disinfectant.

2. *EPA's response.* Since the publication of the proposed rule, the definitions, including those for sanitizer and disinfectant, were published in the **Federal Register** for public comment on January 27, 2010, as part of requesting comment on draft guideline 810.2000. After further review of the comments submitted on the proposed definition for disinfectant and sanitizer, the Agency has revised the definitions that had been proposed for both part 158, subpart W and the 810 Guidelines. EPA believes that the definitions being codified in part 158, subpart W reflect the input received from the regulated community in multiple submissions.

The definition for disinfectant is being revised from, “Disinfectant means a substance, or mixture of substances that destroys or eliminates a specific species of infectious or public health microorganism, but not necessarily bacterial spores, in the inanimate environment” to read, “Disinfectant means a substance, or mixture of substances, that destroys or irreversibly inactivates bacteria, fungi and viruses, but not necessarily bacterial spores, in the inanimate environment.”

The definition for sanitizer is being revised from, “Sanitizer means a substance, or mixture of substances that reduces the bacterial population in the inanimate environment by significant numbers, but does not destroy or eliminate all bacteria or other microorganisms” to read, “Sanitizer means a substance, or mixture of substances that reduces the bacterial population in the inanimate environment by significant numbers, but does not destroy or eliminate all bacteria. Sanitizers meeting Public Health Ordinances are generally used on food contact surfaces and are termed sanitizing rinses.” A 3 log₁₀ reduction is the minimum log reduction needed to make a non-food contact surface sanitizing label claim, and is considered a significant reduction.

The definitions for fungicide, sterilant, tuberculocide and virucide are being revised to include the following phrase: “or mixture of substances.” Inclusion of this phrase in all of the definitions in § 158.2203 for types of products that bear public health claims

(excepting microbiological water purifier) means consistency in the definitions and an acknowledgement that the destroying, reducing, or inactivating may be accomplished via more than a single substance. Also, this makes these definitions similar to the FIFRA section 2(u) definition of pesticide which also contains the phrase “or mixture of substances.”

Additionally, the definition for virucide is being revised to include the word irreversibly, as follows: “Virucide means a substance, or mixture of substances, that destroys or irreversibly inactivates viruses in the inanimate environment,” thus reading similar to the definition for tuberculocide. Additionally, the definition for sterilant will be revised to remove the second sentence of the proposed definition: “For purposes of this subpart, ‘sporicide’ and ‘sterilant’ are synonymous.” EPA no longer requires that products that make sporicidal claims also make sterilant claims.

D. Nonpublic Health Data and Claims

1. *Comment.* A commenter asked that the issue of when to generate efficacy data for nonpublic health products be discussed, since registrants are required to develop data to substantiate label claims.

2. *EPA’s response.* The Agency believes this issue has been addressed in § 158.2220 “Product Performance,” which clearly states, “Each applicant must ensure through testing that his product is efficacious when used in accordance with label directions and commonly accepted pest control practices.” However, to clarify the issue further, the Agency is adding a definition for nonpublic health claims that will appear as 40 CFR 158.2204(b). Additionally, EPA is revising 40 CFR 158.2220(a)(3) to describe that products bearing a nonpublic health claim are to be supported by product performance data.

Also, EPA has posted on the Antimicrobials Division website the parts of the 91 Guideline series that apply to testing of nonpublic health products. Although these

guidelines are from 1982, they are still relied on to develop data to support label claims for nonpublic health products. EPA acknowledges that some of the references in the 1982 guidelines are to the older 91 series guidelines, which is being replaced by the 810 series guidelines. To assist readers, EPA has also posted a cross-walk table so readers can locate the applicable section of the 810 Guidelines. For information, see <http://www.epa.gov/oppad001/non-public-health.html>.

X. Toxicology Data Requirements

The following represent the significant comments received on the need for and evaluation of toxicology studies as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Threshold of Toxicological Concern Approach

1. *Comment.* There should be a threshold of toxicological concern (TTC) type of approach for antimicrobials.

2. *EPA's response.* OPP's Antimicrobials Division is aware of the TTC concept. ILSI is currently pursuing the development of an application of the TTC concept to evaluate antimicrobial pesticides. Development and peer review of a TTC approach for antimicrobials is expected to occur over the next 1 to 2 years. Based on expert peer review and public comment, the Agency will make decisions regarding implementation.

B. Test Note to Neurotoxicity Studies

1. *Comment.* A commenter stated that proposed test note 6 to the proposed toxicology table in § 158.2230 triggering the neurotoxicity studies is contradictory and unclear. The commenter asked how the absence of a neurotoxicity screen in the 90-day oral rodent study would impact proposed test note 6?

2. *EPA's response.* Proposed test note 6 specifies that if the neurotoxicity screen that occurs in the 90-day oral rodent study or any other data demonstrate neurotoxic

effects, then both the acute neurotoxicity study and the 90-day neurotoxicity study are triggered. For certain use patterns with the potential for larger exposures (most notably food exposures), all three of these studies are initially required. According to proposed test note 8 to the proposed toxicology table in § 158.2230, the applicant may combine the 90-day oral toxicity study and the 90-day neurotoxicity study by adding a separate group of test animals.

However, for some use patterns, the 90-day oral study is required, and the other two studies are conditionally required, being triggered by proposed test note 6. EPA acknowledges that when only the 90-day oral study is required, an applicant is at a disadvantage in terms of any chance for combining the 90-day neurotoxicity study with the oral study: Once the 90-day oral study with its neurotoxicity screen has been performed, and neurotoxic effects are identified, then it is not possible to add a separate group of test animals to the already conducted study.

As a point of clarification, EPA is adding a new test note to the final toxicology table in § 158.2230(g) to clarify that the neurotoxicity screen that is part of the 90-day oral study is not equivalent to a 90-day neurotoxicity study. If the 90-day oral toxicity study does not have a neurotoxicity screen, then the acute neurotoxicity study in the rat would be required. The new test note also includes: “if the 90-day oral rodent study does not include a neurotoxicity screen, then the acute neurotoxicity study will be required.” As part of renumbering, this new test note is now test note 11 to the toxicology table in § 158.2230(g) in this final rule.

C. End-Product Use-Dilution Toxicity Testing

1. *Comment.* Several commenters stated their belief that acute end product use-dilution toxicity testing should be optional and requested greater clarification on when to test a diluted product. The commenters asked whether extrapolation from the active ingredient or as-sold acute toxicity testing is acceptable? Another commenter claimed that

requiring end-product six-pack testing of one or more dilutions is duplicative.

2. *EPA's response.* Proposed test note 2 to the proposed toxicology table in § 158.2230, specifies how to conduct acute toxicity testing for end-use products (EP). EP testing is conducted on the product as formulated for sale and distribution. From the EP acute toxicity studies, EPA derives toxicity categories which are then used to determine the precautionary labeling statements on the product. However, it is common for some products to be diluted before being used. The use-dilution testing is in addition to the as-formulated-for-sale testing since there are exposures to both. Acute toxicity testing on the product that has been diluted-for-use supplies the information needed to derive precautionary statements for the user of the product. EPA is revising proposed test note 2 to make this clearer.

D. The Phrasing "limited portion of the human lifespan"

1. *Comment.* Several commenters asked EPA to identify the criteria to determine "repeated human exposure over a limited portion of the human life span." They asked EPA to specifically describe what the phrase "human exposure is not purposeful" means?

2. *EPA's response.* Proposed test note 11 to the proposed toxicology table in § 158.2230, specifies the triggers that would require the performance of a 90-day oral study in the non-rodent. EPA has reevaluated this test note and decided not to codify test note 11, as proposed, Proposed test note 11, subparagraph i. contained the phrase "repeated human exposure over a limited portion of the human life span." EPA agrees that this phrase is not useful. Proposed test note 11, subparagraph ii. contained a trigger for any indirect food use that would have been considered to be a "low exposure." Given the restructuring of the final toxicity data requirements table, i.e., the shift away from using high and low exposure as the table headers to a food/nonfood approach, test notes 11, subparagraphs i. and ii. are no longer needed. In the final toxicity table in § 158.2230(g), the data required for an indirect food-use is specified directly (in the table header) and a

trigger is not needed.

Test note 12 to the proposed toxicology table in § 158.2230, specifies three triggers that would require the performance of a 21/28-day dermal study. EPA has also reevaluated proposed test note 12 and agrees that the phrases “repeated human exposure over a limited portion of the human life span” and “human exposure is not purposeful” are not useful. Accordingly, EPA has revised the 21/28 day dermal study trigger. The 21/28 day dermal study is now triggered if all of the following criteria are met:

- i. The intended use of the antimicrobial pesticide product is expected to result in repeated dermal human exposure to the product;
- ii. Data from a 90-day dermal toxicity study are not available;
- iii. The 90-day dermal toxicity study has not been triggered (the third proposed trigger).

E. Mouse Carcinogenicity Study

1. *Comment.* According to several commenters, the mouse carcinogenicity study does not provide useful information, and is, in fact, not suited for determining/extrapolating human carcinogenicity. They contended that EPA should no longer require the mouse carcinogenicity study. This would also mean that there is no need for the mouse range-finding study.

2. *EPA's response.* The issue regarding the usefulness of the mouse for carcinogenicity testing is one that is currently under debate by the OPP. Currently, carcinogenicity testing, whether for conventional pesticides under § 158.500 or for antimicrobials under part 158, subpart W requires testing in two rodent species. However, OPP is currently conducting a comprehensive analysis of its rodent chronic bioassay database to document the utility of the mouse bioassay for both cancer risk assessment and Reference Dose (RfD) derivation for non-cancer endpoints. When this analysis is completed, a recommendation will be made regarding the testing needed for cancer hazard

identification. Once OPP's internal review process is complete, then it is likely that EPA would solicit review and comment by the FIFRA SAP. If at a later date, the determination is made to alter the carcinogenicity data requirements, then appropriate changes would be proposed to be made to data requirements and regulations pertaining to conventionals, biochemicals and microbials, and antimicrobials through rulemaking.

F. Ames Assay

1. *Comment.* A commenter argued that the Ames assay should not be required, because it is inappropriate for antimicrobials that kill bacteria.

2. *EPA's response.* It is recognized that the Ames assay may not be useful for assessment of mutagenic potential of antimicrobial pesticides, as this test uses strains of bacteria as the primary test material, and antimicrobials are designed to kill, among other things, bacteria. So, the bacteria may be killed before mutagenic effects are demonstrated. However, for some antimicrobial pesticides, the Ames assay has already been conducted and if the Ames assay was conducted at levels that do not cause toxicity to the bacterial strains tested, then the study may be acceptable to fulfill the reverse mutation assay requirement. However, if an Ames assay has not yet been conducted for a particular antimicrobial, then, the Ames assay should not be conducted. In this final rule, test note 32 for the reverse mutation assay requirement in the final toxicology table in § 158.2230(g), is revised to allow reliance on previously-conducted Ames tests when the bacteria strain was not killed, but to state a preference for assays such as an *in vitro* mammalian cell assay, (e.g., the mouse lymphoma TK +/- assay).

G. Dermal Absorption Studies

1. *Comment.* A commenter argued that EPA should accept *in vitro* skin penetration data. According to the commenter, accepting such data would harmonize with requirements in the European Union (EU) and elsewhere. The commenter pointed to well-established OECD guidelines for these studies. The commenter also asserted that proposed

test note 37 to the proposed toxicology table in § 158.2230, addressing the requirement for a dermal absorption study, should not apply to corrosive/irritant products.

2. *EPA's response.* The Agency has, on a case-by-case basis, used *in vitro* dermal absorption studies to determine the magnitude of dermal absorption of pesticide chemicals. However, the Agency has not adopted an official policy of using only *in vitro* data to support these decisions. OECD guideline 428, while describing an *in vitro* method for dermal absorption, does not rule out the use of *in vivo* data along with *in vitro* data to determine dermal absorption. Further, the test guideline notes that formal validation studies of the *in vitro* method have not been performed.

The Agency is working on developing a more formal policy that would use both *in vivo* and *in vitro* dermal penetration data in a weight-of-evidence (WOE) determination in appropriate cases. The Agency would always consider QSAR or other models, submitted in support of the determination of dermal absorption. The decision to accept such information is the Agency's, based on its review and evaluation of the submission.

Test note 37 to the proposed toxicology table in § 158.2230, specifies that the trigger for requiring a dermal penetration study are the results from a risk assessment "assuming that dermal absorption is equal to oral absorption." This means that EPA assumes 100 percent dermal absorption. If a subchronic dermal study and/or dermal absorption data are not available, then a risk assessment could be conducted using the default assumption of equivalent absorption by the dermal and oral routes of exposure. If unacceptable risks are found, then either the subchronic dermal study or a dermal absorption study would be required. EPA recognizes that the assumption of 100 percent dermal absorption is conservative; however, this assumption would only be used in the absence of an acceptable dermal subchronic study or dermal absorption data. In this final rule, test note 37 to the toxicology table in § 158.2230(g), is revised to clarify this process. EPA also agrees that corrosive/irritant products should not be tested in dermal absorption

studies. Therefore, test note 3 to the toxicology table in § 158.2230(g), which specifies that testing is not needed for corrosive materials, is added as a trigger for not requiring the dermal absorption study.

H. Tiering

1. *Comment.* One commenter argued that EPA has not provided meaningful tiering for its toxicology requirements for antimicrobials. Another commenter claimed that exposure alone is not an appropriate criterion to use for a tiered testing scheme, that both exposure and risk should be considered. A third commenter asserted that the high and low human exposure categories for toxicity are not appropriate and suggested that a tiered scheme such as that used for environmental fate data requirements would be more appropriate.

2. *EPA's response.* In its proposed rule EPA proposed a tiered testing scheme for toxicology testing that was based on the amount of exposure as defined by use patterns. Based on its experience in conducting risk assessments, EPA understands which use patterns have exposures of higher duration and magnitude, and therefore could have greater risks. Use patterns with higher exposures require submission of more data than use patterns with lower exposures.

I. Guideline Numbers in the Code of Federal Regulations

1. *Comment.* A commenter stated that the final rule should not specify a guideline number. Instead, the data requirement tables should describe the endpoint in question, and the information needed for EPA's risk assessment. OPP could develop guidance that could be placed on the web.

2. *EPA's response.* The guideline number column could be removed from the table. Instead, EPA could have an internet page that describes multiple methods of fulfilling the data requirements. An internet table could be updated faster to reflect newer techniques than rulemaking to revise a regulation in the CFR. However, there is also value

in having the guideline number in the CFR, which then shows the available guidelines relevant to the particular study that should be considered in addressing the requirement. EPA has made no decision on whether or not to initiate a rulemaking to remove all the guideline numbers from the data requirement tables in 40 CFR part 158. The tables finalized in subpart W in this rule include guideline numbers.

J. Animal Testing

1. *Comment.* A commenter requested that EPA specifically state in its regulations that non-animal methods are acceptable for fulfilling a data requirement. The commenter argued that the Draize study (the acute eye irritation study) in rabbits should be eliminated.

2. *EPA's response.* Non-animal test methods are continually being examined for use in fulfilling the toxicology data requirements that are used to assess the hazard of pesticide chemicals. However, in order for non-animal approaches to be used for fulfilling toxicology data requirements, these approaches must first be scientifically validated to ensure that they are as good as the existing test method for predicting hazard and also assessed to determine whether they meet the Agency's "3 R" goals of reduce, refine, and replace the use of animals in testing. With respect to antimicrobial pesticides, the Agency has started to explore such approaches. One example of this is the voluntary pilot program for eye irritation testing of antimicrobial pesticides using non-animal test methods, found at <http://www.epa.gov/oppad001/eye-irritation.pdf>.

K. Derivation of 200 parts per billion Criterion

1. *Comment.* A commenter asked whether the 200 parts per billion (ppb) level used as the dividing line between high and low human exposures is the concentration of a substance in an adult's daily food consumption?

2. *EPA's response.* The derivation of the 200 ppb level was previously established by FDA for indirect food use biocides (identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0010). FDA derived the 200 ppb level by dividing the

cumulative exposure upper limit of 1,000 ppb for food contact substances by 5 to account for the fact that antimicrobial pesticides (e.g., biocides) are a class of pesticide that are generally toxic by design. The 200 ppb level is the concentration of the antimicrobial residues in or on the food item. EPA is using 200 ppb as a delineation consistent with the FDA's toxicology recommendations for food contact substances. Therefore, those indirect food uses that have residues that are less than or equal to 200 ppb in or on the food item usually have fewer data requirements than those that have residues that are greater than 200 ppb in or on the food item. For clarity, information concerning the 200 ppb level and its derivation from FDA levels has been added to § 158.2230(d).

L. Use of OECD Guidelines for EPA Registrations

1. *Comment.* A commenter asked EPA to consider incorporating the following OECD guidelines into the new part 158, subpart W to reduce the number of animals killed in LD₅₀ tests: OECD guidelines 436; Acute Inhalation Toxicity - Acute Toxic Class Method, and revised 223; Avian Acute Oral Toxicity Test, and Short Guidance on the Threshold Approach for Acute Fish Toxicity.

2. *EPA's response.* OPP does not have a policy for use of OECD 436 for acute inhalation toxicity. If a study conducted according to OECD 436 were submitted for the purpose of assessing acute inhalation toxicity, EPA would review and accept the results if the study were conducted in an acceptable manner and provided sufficient information to fulfill the data requirement. Similarly, if a study conducted according to OECD 223 or the Threshold Approach, were submitted, then EPA would review the study and then make a determination on whether the study was conducted in an acceptable manner and provided sufficient information to fulfill the data requirement.

M. Alternative Formats for Toxicology Data Requirements Table

1. *Comment.* In the comments submitted to EPA, the commenters suggested two

alternative toxicity data requirement approaches for EPA to consider. Alternative approach 1 was organized in paragraphs and alternative approach 2 was in a table format similar to that proposed by EPA.

2. *EPA's response.* The commenters provided two alternative approaches for toxicology data requirements for antimicrobials. As stated by the commenter, alternative approach 1 was “intended to provide clearer instructions to registrants,” attempted “to fully incorporate the new science” of integrative approaches to testing, and included “a threshold concept for toxicological concerns.” (ACC Comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.6; Appendix E, entitled “Comments on Proposed Data Requirements for Toxicology” p. 24). The commenter did not provide to EPA the same or similar table-type of format used for part 158 data requirements. There were no test notes to define the triggers for moving from tier to tier. The commenter acknowledged that their suggested alternative approach 1 would require “expert scientific judgment” (p. 25), and also discussed that EPA in the proposed rule (73 FR 59423) had indicated the need to develop scientific position papers, and recommendations for internal and external review of integrative approaches. EPA considers alternative approach 1 to be a dramatic departure from EPA’s proposal, and agrees with the commenter that certain scientific issues may not be ready for codification. EPA does not believe, at this time, that this approach meets the needs of the Agency, or has any advantages over the table format. EPA found the paragraph explanations unclear. As acknowledged by the commenter, the paragraph format would result in a more complex decision tree that would require a significantly greater amount of interpretation and consultation when compared to the existing table formats. There would be a significant learning curve for both EPA and those members of the public that have become accustomed to data requirement tables such as in part 158. Within this response, EPA has responded to alternative approach 1 in totality. EPA notes that the individual scientific issues raised within the paragraphs are addressed

separately, as they were separated into the various disciplinary areas of the toxicology comments.

EPA has also evaluated alternative approach 2. This alternative approach is in a table-type of format with a strict split between food and nonfood uses. The test notes developed by the commenters are extremely detailed and contain information that EPA believes is more appropriate in guidance. However EPA has used the suggested test notes to revise the test notes in this final rule as appropriate. For example, the commenters' suggested test note 32 to the *in vivo* cytogenetics study is clearer than EPA's proposed test note 34. Therefore EPA is revising test note 34 to the final toxicology table in § 158.2230(g), accordingly.

As discussed previously, as a result of comments received, EPA is no longer using the terms "high human exposure" and "low human exposure" as proposed for the antimicrobial toxicology data requirements table. Instead, in the final rule, EPA is now using a food/nonfood approach with some similarities to that of the toxicology data requirements table for conventional pesticides to distinguish the use patterns with higher exposure that need more toxicity data from those that need less. Accordingly, the table headers for the toxicology data requirements table in the final rule are: "Direct Food Uses;" "Indirect Food Uses (>200 ppb);" "Indirect Food Uses (≤200 ppb);" "Swimming Pools, Aquatic Areas, Wood Preservatives, Metal Working Fluids;" and "All Other Nonfood Uses."

Unlike conventional pesticide chemicals, a strict food/nonfood use "split" for delineating data requirements is not appropriate for antimicrobial chemicals. Such an approach does not fully address the unique use patterns for antimicrobials, most specifically, those involving indirect food uses. As a result of comments received, EPA decided to employ a modification of the food/nonfood approach to delineate the specific data requirement needs for antimicrobial pesticides.

The commenter has also asked that EPA include within subpart W a new § 158.2235 which would be analogous to 40 CFR 158.510 for conventional chemicals (Tiered Testing Options for Nonfood Use Pesticides). EPA does not believe this is needed for antimicrobials. Once it has been determined that the use is nonfood, then certain of the nonfood use scenarios require the submission of more data, and certain require the submission of less data. As specified in the column headings for Nonfood Uses, swimming pools, aquatic areas, wood preservatives, and metal working fluids require a particular set of data. All other nonfood uses require less data. Thus, the tiering is already built into the approach used for antimicrobials.

XI. Nontarget Organism Data Requirements

The following represent the significant comments received on the need for and evaluation of nontarget organism studies as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Need for Ecotoxicity Data for Indoor Uses

1. *Comment.* Several commenters argued that there are few antimicrobial use patterns where ecological effects information would be relevant to an assessment under FIFRA because there is no expectation of environmental exposure.

2. *EPA's response.* As explained in the proposed rule, there is now a greater concern regarding indoor uses of antimicrobials because those uses can lead to environmental exposure when they go down the drain. The Agency and the scientific community have become concerned with pharmaceuticals and personal care products (PPCPs), which are now recognized as environmental contaminants. A subset of these PPCPs includes antimicrobial pesticide products, some of which are being detected in various environmental compartments/media [e.g., surface water and WWTP biosolids]. As discussed in the proposed rule (73 FR 59407), these findings are notable, because many of

the antimicrobial pesticides detected are registered for only indoor use patterns.

There are many uses for which a high potential for environmental exposure exists, especially outdoor uses such as wood preservatives, ballast water treatments, antifoulant paints and coatings, aquatic areas, and others. These uses may require a more extensive data set that could include acute and chronic tests in both freshwater and saltwater, and possibly in the sediment as well as the water column. If the effluent from a WWTP is likely to contain an antimicrobial pesticide, or if the antimicrobial is likely to partition to the sludge that is derived during the treatment process, then indoor uses could require additional testing to further characterize the hazard and the risk.

B. Transformation Products

1. *Comment.* Several commenters questioned, how a registrant would determine if “transformation products” would need to be tested. With regard to the criteria for when testing is required on transformation products, another commenter stated the belief that any data developed to assess the potential risk to nontarget organisms should be developed with the appropriate residue of concern (ROC) (i.e., degradation product, metabolite, or TGAI) rather than always testing with the TGAI. Still another commenter asked how would EPA determine that the transformation products are “more toxic, persistent, bioaccumulative or have been shown to cause adverse effects in mammalian or aquatic reproductive studies.” Finally, a commenter requested that EPA explain what is considered “stable” in the environment in proposed test note 3 to the proposed nontarget organism table in § 158.2240.

2. *EPA’s response.* The Agency evaluates the need for nontarget organism testing of transformation products on a case-by-case basis, using several sources of information, which includes, most importantly, environmental fate data. EPA proposed to require nontarget organism testing of transformation/degradation products or leachate residues in proposed § 158.2240(a)(3) and (4). To respond to this comment, EPA also considered a

similar comment on transformation/degradation products or leachate residues for environmental fate testing (see Unit XIV.B.). In response to these comments, EPA determined to clarify and revise the criteria for testing of transformation/degradation products and leachate residues for nontarget organisms in §158.2240(a)(3), for environmental fate in §158.2280(a)(2) and for nontarget plant protection in §158.2250(b).

As explained in Unit XIV.B., environmental fate studies provide information on the stability and persistence of the active ingredient and degradation products in the various environmental media. If the environmental fate studies on the parent indicate the transformation/degradation product(s) is, for example, more persistent in soils, then it is possible that nontarget plants or animals could be exposed to the degradate. Once the transformation products and the environmental compartment in which they occur are identified, then the available toxicology data (e.g., reproduction tests, developmental tests, non-rodent chronic studies) are reviewed to determine toxicity.

After reviewing all available information, then EPA would use these criteria to determine if ecological effects data on the transformation/degradation products or leachate residues are required for either nontarget organisms or nontarget plants. EPA believes that nontarget plant protection data may sometimes be needed when the Agency begins conducting species-specific endangered species assessments for antimicrobial pesticides.

EPA does not use the term “residue of concern (ROC)” in the final Nontarget Organisms Data Requirements Table. Instead, the appropriate test material(s), such as TGAI, degradate, or TEP, is specified in the data requirements table in § 158.2240. This approach is also used for the conventional nontarget organism table in part 158. Generally, for ecological testing, the TGAI testing is performed first, and then additional testing on a transformation product may be required based on the process described previously. Depending on how fast a substance decays, a nontarget organism or plant could actually be

exposed to a mixture of the parent and one or more degradation/transformation products.

C. Test Note 7 to the Nontarget Organism Table and Wood Preservatives

1. *Comment.* Test note 7 to the proposed nontarget organism data requirements table in § 158.2240 specifies the triggers for requiring typical end-use product (TEP) testing for the acute freshwater invertebrate study and acute freshwater fish study. A commenter asked whether, even though, the wood preservatives use pattern is specified as “NR,” could the TEP testing be required because of the triggers in test note 7.

2. *EPA’s response.* Proposed test note 7 also triggered the testing for the TEP acute estuarine and marine organisms toxicity testing. EPA agrees that the combination of “R”s, “CR”s, “NR”s and the current structure of proposed test note 7, is confusing and that clarification is needed.

The data requirements for TEP testing and proposed test note 7 were also considered in light of the Agency’s determination based on comments received (see Unit VI.B.) on EPA’s current practice of conducting risk assessments for wood preservatives based on land-only versus a land and aquatic predetermined use pattern. All wood preservative risk assessments will now be performed considering that the treated wood could end-up on both the land or in the aquatic environment. As previously discussed, there are multiple pathways for wood preservative degradates and/or leachates to reach surface water. EPA has also determined to conduct a down-the-drain assessment for all appropriate use patterns which would include wood preservatives, and antifoulant paints and coatings (see Unit XV.A.). For wood preservatives, these determinations mean that additional ecological testing is required to conduct an ecological risk assessment, and the following changes are made to the wood preservative testing column:

- Acute freshwater invertebrates toxicity (TEP testing): change from “NR” to “CR”;

- Acute freshwater fish toxicity (TEP testing): change from “NR” to “CR”;
- Acute estuarine and marine organisms toxicity (TEP testing): change from “NR” to “CR”.

For antifoulant paints and coatings, the determination to conduct assessment also means that additional data could be needed for the down-the-drain assessment, and the following changes have been made to the antifoulant paints and coatings testing column:

- Acute freshwater invertebrates toxicity (TEP testing): change from “NR” to “CR”;
- Acute freshwater fish toxicity (TEP testing): change from “NR” to “CR”;
- Acute estuarine and marine organisms toxicity (TEP testing): change from “NR” to “CR”.

EPA believes that simplifying the data requirements that reference test note 7 to the final nontarget organism table in § 158.2240(c) so that these requirements are CR for all use patterns is clearer, and also closer to the suggestions made by the commenters in their suggested nontarget organism data requirements table. Their suggested table was predominantly “CR” for aquatic uses. Therefore, in this final rule, test note 7 triggers the “CR” studies.

However, changing all the use patterns to “CR” for the TEP studies means changing the “R” proposed for the aquatic use, and industrial processes and water systems use patterns for the acute freshwater invertebrates toxicity study and the acute freshwater fish toxicity study, to “CR.” To account for this change proposed test note 7 to the proposed nontarget organism table in § 158.2240 has been revised in the final rule to include an additional trigger (see §158.2240(d) test note 7.iv). Data are required when “the end-use antimicrobial product will be applied directly into an aquatic environment.” EPA believes that the implications of this trigger are equivalent to the “R” and essentially this is

a non-change. These changes are summarized here for both the aquatic areas and industrial processes and water systems testing column:

- Acute freshwater invertebrates toxicity (TEP testing): change from “R” to “CR”;
- Acute freshwater fish toxicity (TEP testing): change from “R” to “CR”;
- Acute estuarine and marine organisms toxicity (TEP testing): no change.

Nontarget organism toxicity testing of the TEP should be infrequently required for the antifoulant paints and coatings use pattern because for this use pattern, the TEP could be the paint. Because the testing for aquatic organisms is done in water, the test material must be soluble in water, or made soluble by addition of an appropriate solvent, if one exists, or other appropriate mechanical methods. Paint is not soluble and there may not be a way to make it soluble. Since these studies are often run in glass aquaria, the paint could coat the sides of the glass and the test animals themselves. The paint could ruin test equipment by clogging lines and injection nozzles. Therefore EPA has added a new test note 5, which is replacing proposed test note 5 to the proposed nontarget organism in § 158.2240. New test note 5 to the final nontarget organism table in § 158.2240(c) states that an applicant should request a waiver if the TEP cannot be tested.

EPA also notes that a test note specifying the number of species to be tested was omitted in the proposed rule for the TEP testing for acute freshwater fish toxicity. This test note is needed for clarity. Test note 3 to the final nontarget organism table in § 158.2240(c) has been added to the line for acute freshwater fish toxicity. Instead of “greater than 1 ppm or 1 mg/L” as indicated in the proposed rule, the toxicity trigger has been corrected to read “less than or equal to 1 ppm or 1 mg/L.” If the LC_{50} is greater than 1 ppm this means that the chemical tested was moderately to practically non-toxic on an acute basis. If the LC_{50} is less than 1 ppm this means that the chemical tested was highly

to very highly toxic on an acute basis and would have a serious adverse affect(s) on the organism tested at low concentrations. For clarity, in test note 3 to the nontarget organism table, EPA has specified the appropriate trigger (less than or equal to) to indicate that testing is needed for chemicals that demonstrate high to very high toxicity on an acute basis.

D. Acute and Chronic Toxicity Data

1. *Comment.* A commenter argued that it is essential to have both acute and chronic toxicity test results for at least one freshwater invertebrate, vertebrate, and plant species, and at least one marine/estuarine invertebrate, vertebrate, and plant species.

2. *EPA's response.* EPA proposed to require acute tests for both a cold water and warm water freshwater fish, an invertebrate, and one or more aquatic plants. For marine/estuarine species, for most use patterns, EPA proposed to conditionally require acute testing with a fish and two aquatic invertebrate species, including a bivalve, when the Agency believes there is a potential for the active ingredient or a potentially toxic degradate to reach the estuarine/marine environment through transport (e.g., leaching, runoff) from the treatment site. In such a situation, chronic testing with one or more marine/estuarine species also may be required if the Agency believes that chronic exposure is likely. These studies also are required for those uses where the pesticide product is applied directly into the marine/estuarine environment.

As to chronic testing, EPA proposed to require the fish early life stage and the aquatic invertebrate life-cycle studies for the industrial processes and water systems (once-through), antifoulant coatings and paints, and aquatic areas use patterns. At that time, EPA also proposed to conditionally require the same two studies for the low environmental grouping (now called the all other use patterns category) and wood preservatives.

However, based on this and other comments, EPA has reevaluated the nontarget organism data needed for a registration decision and concluded that additional acute and

chronic data are needed. Plant species encompass many different life spans. Phytoplankton reproduce quickly and have extremely short life spans. Annuals live for 1 year. Many perennials do not actually live for multiple years, but reproduce from seeds year after year. The plant species that live the longest would be woody species, such as trees. EPA does not believe that antimicrobial use patterns impact terrestrial areas such that chronic exposures occur. To EPA's knowledge, no adverse chronic effects to terrestrial plants caused by pesticides have been documented on plants. Any effect on terrestrial plant species has been categorized as an acute effect and would be covered by current testing procedures. Chronic effects of aquatic plants are covered by the aquatic testing guidelines. Algae are used as the primary test species for evaluating effects to the aquatic plants. The testing is based on growth parameters and the tests normally run for periods of time that would include several generations of the algae. The results from these algal studies, while only conducted over a few days, would be similar to those obtained from chronic testing in other species, and would be used to assess any chronic effects to aquatic plant species.

E. Avian Studies

1. *Comment.* In proposed test note 4 to the proposed nontarget organism table in § 158.2240, which triggers the avian dietary study, EPA specified a trigger of 100 mg a.i./kg (milligrams active ingredient/kilogram) for additional testing. A commenter requested information on why this trigger was selected. The commenter also claimed that EPA could use exposure tools to conduct an initial assessment based on Tier I data, and then trigger additional testing based on risk.

2. *EPA's response.* OPP has long used this value as an indication of toxicity to birds. As specified in 40 CFR 156.85(b)(3), any pesticide (including conventional pesticides) that is intended for outdoor use with an avian acute oral LD₅₀ of 100 mg a.i./kg or less requires a precautionary label statement that the pesticide is toxic to birds. EPA believes that if 100 mg a.i./kg is appropriate to trigger a precautionary label statement, then

it is also appropriate to use as a trigger for testing. Therefore, if the avian oral acute toxicity study indicates an oral LD₅₀ of 100 mg a.i./kg or less, then an avian dietary study is required.

In the proposed rule, for the avian dietary toxicity study, EPA proposed to require testing on two species for the aquatic areas and to conditionally require testing on one avian species for all of the other use patterns. The comments reviewed and evaluated by EPA on avian toxicity testing included the commenter's suggested data requirements table for nontarget organisms, which specified "CR" for all avian testing. EPA agrees with the commenter that "CR" is appropriate for the avian dietary toxicity and avian reproduction studies for all use patterns. This simplifies the test notes and with the appropriate triggers EPA would be able to require the needed testing.

The following changes have been made to the aquatic areas column:

- Avian dietary toxicity: change from "R" to "CR";
- Avian reproduction: change from "R" to "CR".

Test note 4 to the final nontarget organism table in § 158.2240(c) triggers the avian dietary toxicity study based on the results of the avian acute toxicity study. For the avian dietary study, testing in a second species would be triggered based on the results of the avian dietary testing in the first species. Since the second test species will be required, based on the results of the first species, proposed test note 5 is no longer needed and is being removed. Test note 6 to the final nontarget organism table in § 158.2240(c) would trigger the avian reproductive study based on one or more of four specific criteria. There were no revisions to these criteria from the proposed rule to the final rule.

F. Water Quality Criterion

1. *Comment.* A commenter argued that the registrants of any antimicrobial pesticide that has the potential to be discharged either directly or indirectly to surface water

should be required to supply any additional data needed to derive a water quality criterion for the pesticide in question.

2. *EPA's response.* As discussed in the conventionals' Response to Comments Document in docket EPA-HQ-OPP-2004-0387 (p. 104), the Agency's pesticide registration process, including its data requirement regulations, adequately considers the endpoints that are protected under the Clean Water Act (CWA) as administered by the Office of Water (OW). When acceptable data are available, OPP uses these data in its risk assessment process.

The purpose of a water quality criterion under the CWA is to determine the level at which a water body may be at risk for environmental damage. The purpose of certain data requirements for pesticide registration is to allow the Agency to determine the ecological risk of using a pesticide. Thus, these program offices within EPA have similar goals. While EPA has developed guidelines for developing Water Quality Criteria (WQC), the Agency has also recognized that WQC can be developed with a more limited data set.

Pesticide registration data are valuable in assessing water quality risks. As noted in EPA's 2005 Response to Comments Document on the conventional pesticides, EPA's OW and OPP together developed aquatic life benchmarks for 71 pesticides or pesticide degradation products for States to use to establish targets for safe levels of pesticides for aquatic plants and animals. The benchmarks are derived from data submitted to EPA for pesticide registration. As of April 18, 2011, there are 242 pesticide chemicals with aquatic benchmarks on EPA's website

(http://www.epa.gov/oppefed1/ecorisk_ders/aquatic_life_benchmark.htm).

G. Sediment Testing

1. *Comment.* The commenter asserted that EPA did not consider the environmental fate of a compound (such as the tendency of a chemical to absorb/desorb) when considering the need for sediment testing.

2. *EPA's response.* EPA disagrees with this comment. Test notes 17 and 18 to the final nontarget organism table in § 158.2240(c) trigger the sediment studies based on the results of the aerobic soil or aquatic metabolism studies and knowledge of the physical/chemical properties which express the environmental fate of the antimicrobial pesticide chemical. The soil partition coefficient (K_d) is used as an expression of the binding capability of the chemical to sediments. The Agency's justification for using $K_d \geq 50$ as a criterion for requiring sediment testing is that this value would capture those chemicals with about 80 percent adsorption to sediments (relative to organic carbon).

The octanol-water partition coefficient (K_{ow}) and the soil organic carbon-water partition coefficient (K_{oc}) also are used by EPA as part of its decision process. Both values are frequently more available than either the K_d or half-life values. Test note 17, the trigger for requiring an acute sediment study, considers all four of these values.

Next, as explained in test note 18, the chronic sediment study is triggered based on the results of the acute sediment study as well as a reexamination of the K_{ow} , K_{oc} , and K_d .

XII. Nontarget Plant Protection Data Requirements

The following represent the significant comments on the need for and evaluation of nontarget plant protection studies as proposed by EPA. The changes from the proposed rule to final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Triggers for Higher-Tiered Plant Studies

1. *Comment.* One commenter asked EPA to explain the criteria used to trigger higher-tiered plant studies based on the results of the algal studies.

2. *EPA's response.* The criteria to trigger higher-tiered plant studies are specified in test notes 2 and 5 to the proposed nontarget plant protection table in § 158.2250. A toxicity level ($EC_{50} < 1$ ppm) indicates that the antimicrobial pesticide would have serious adverse affect(s) on algae at low concentrations. This could have serious consequences to

nontarget algae species. Therefore, at this toxicity level, additional higher-tiered testing is required to further characterize the potential adverse affects to aquatic plants. EPA is retaining the toxicity trigger of <1 ppm in test note 5 to the final nontarget plant protection table in § 158.2250.

In evaluating test note 2 to the proposed nontarget plant protection table in § 158.2250, EPA has considered the commenter's suggested table for nontarget plants. For the seedling emergence study, the commenter used "CR" for most use patterns and suggested that the seedling emergence study should only be required "when environmental exposure is likely to result under normal usage conditions as determined by appropriate assessment methods." Another comment (see response to comment 140.27 in the Response to Comments Document in the docket) advocated for the use of a Risk Quotient (RQ) approach for assessing plants.

Based on this evaluation, EPA believes using "CR" for the seedling emergence study when triggered by a level of concern approach (RQ approach) would provide EPA with the required data when needed. Test note 2 to the final nontarget plant protection table in § 158.2250 now reads as: Data are required if the risk quotient from any aquatic plant growth Tier II study exceeds a level of concern for aquatic plants.

However, test note 2 also triggers the aquatic plant growth (aquatic vascular plant) study, and is still the appropriate trigger for that study. With this final rule, EPA is adding a new test note 10 to the final nontarget plant protection table in § 158.2250, which will read the same as the original, proposed test note 2 to the proposed nontarget plant protection table in proposed § 158.2250.

B. Alternative Format for Plant Protection Data Requirements Table

1. *Comment.* In the comments submitted to EPA, the commenters suggested an alternate antimicrobial plant protection data requirements table.

2. *EPA's response.* The table suggested by the commenter is not adequate to

evaluate the hazards and risks to nontarget plants from antimicrobial pesticides. The suggested table did not include test guideline numbers, changed and reduced the number of use patterns, and proposed that all ecotoxicity plant studies are either not required or only conditionally required. The commenter contends that there are no circumstances where ecological effects plant data are relevant for antimicrobial pesticides, and that indoor uses should not be subject to environmental exposure or nontarget plant species risk assessments. EPA disagrees with many aspects of these comments and the suggested ecotoxicity data requirements table for plant species.

As previously discussed, in the preamble to the proposed rule (73 FR 59406-7) and in Units III. and V. of this rule, EPA disagrees that exposure for nontarget plants should be presumed to be minimal or nonexistent for antimicrobials applied indoors, or that tests are not required if the test organism is the target species for the pesticide (see ACC comment, identified in the docket by document ID No. EPA-HQ-OPP-2008-0110-0088.7, p. 12, test notes 1 and 2 to the commenter's suggested table). Moreover, there are many outdoor uses of antimicrobials that are not addressed in the commenter's suggested table. FIFRA mandates that EPA conduct a risk assessment for any uses for which exposure may occur in the various environmental compartments/media. Those risks are assessed separately for the various taxa, including plants, categories (e.g., freshwater, saltwater), and short-term (i.e., acute) and longer-term (i.e., chronic) exposures. Assessing these potential risks necessitates having an appropriate ecotoxicity data base for plant exposure and toxicity. This can only be accomplished by requiring plant studies for the initial assessment. A tiered approach cannot be driven solely by risk quotients derived from a Tier I study. The fact that an acute risk quotient for a plant species does not exceed a level of concern for acute risk does not imply that a chronic risk does not exist or that data are not needed to assess that risk. The trigger for a chronic test is more likely driven by the frequency, duration, or magnitude of the chronic exposure and the environmental properties of the

pesticide. For example, plants might be subjected to repeated low-level exposure that is not acutely lethal but which may impact reproductive success and plant growth.

EPA disagrees that the test substance for plant studies (in the commenter's table) should be identified simply as the "residue of concern (ROC)." In its proposed nontarget plant data requirements table, EPA specified the test material (TGAI, TEP) to be used for each study. The test substance determination is made after reviewing the required environmental fate and physical/chemical properties data and any other available information (e.g., open literature, closely related chemicals) to determine the substance of concern for exposure of non-target plants and organisms. For example, if an applicant can adequately demonstrate that the TGAI dissipates so rapidly that there would be no acute or chronic exposure, TGAI testing may be waived, and instead degradate testing may be required.

The commenter also omitted all guideline numbers from its suggested data table. At this time, all data requirement tables in 40 CFR part 158 have guideline numbers since this is a method of providing information to applicants. Applicants are not required to use these guidelines, but are encouraged to use these test guidelines when developing data. Since these guidelines have been developed via a rigorous process, as discussed in the preamble to the proposed rule [73 FR 59387], "they represent the recommended approach to developing high-quality data that should satisfy EPA's data needs for risk assessment."

XIII. Applicator and Post-Application Exposure Data Requirements

The following represent the significant comments received on the need for and evaluation of applicator and post-application exposure studies as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Consistency With OSHA and Other Standards

1. *Comment.* A commenter asserted that EPA should be consistent with OSHA and other standards with regard to exposure limits and handling practices, and incorporate the OSHA standards into risk assessment evaluations. The commenter also asked that when EPA believes that an OSHA or American Conference of Governmental and Industrial Hygienists (ACGIH) standard is not adequately protective for an antimicrobial, that the finding should be substantiated.

2. *EPA's response.* The OSHA workplace standard is the permissible exposure limit (PEL). When developing a PEL, OSHA considers the toxicity of the chemical, often using data from the open literature as well as the feasibility that exposures could be reduced to the PEL using process modifications, engineering controls and personal protective equipment (PPE). Approximately 500 PELs have been established.

The ACGIH establishes health-based Threshold Limit Values (TLVs), which are non-governmental guidelines used by professional industrial hygienists in making decisions about safe levels of exposure to a chemical substance in the workplace. The TLVs were established for some chemicals as early as 1946 and they are updated on a regular basis as new health effects information becomes available. Like the OSHA PELs, the TLVs are based on health effects data from the open literature. However, unlike the OSHA PELs, feasibility issues are not considered in establishing TLVs. TLVs are not available for most pesticide chemicals.

However, for those pesticide chemicals with both TLVs and RfCs (Reference Concentrations are established by OPP based on studies submitted by the registrants), the RfCs are often lower than the TLVs. There could be several reasons for such differences. The data used by OPP is submitted by the pesticide registrants and the toxicity data base is composed of animal studies. So, uncertainty factors are used to derive the RfCs (exposure limits). Instead of animal studies, ACGIH prefers to rely on epidemiology studies/case reports of human, particularly worker, exposures from the literature and on professional

judgment.

For example, ACGIH and OPP established different inhalation limits for formaldehyde based on slightly different interpretations of the same literature studies. The TLV for formaldehyde is 300 ppb and the OPP “RfC” for occupational uses is 100 ppb. Although the TLV is greater than the “RfC,” ACGIH does acknowledge in their TLV documentation that irritation can occur in some workers at levels of 100 to 300 ppb.

EPA believes that an existing OSHA or ACGIH standard should be considered as part of EPA’s hazard evaluation. However, before using an OSHA or ACGIH standard, EPA would review the standard and the health effects (toxicology) documents supporting the standard’s development to determine if EPA believes that the standard provides adequate protection. EPA agrees with the commenter that EPA’s evaluation of an existing OSHA or ACGIH standard should be part of its hazard evaluation documentation.

In its proposed rule, EPA proposed in the applicator exposure table (40 CFR 158.2260(a)(1)) and the post-application exposure table (40 CFR 158.2270(a)(1)) to use established workplace standards, such as OSHA’s. The proposed language was:

If EPA determines that industrial standards, such as the workplace standards set by the Occupational Safety and Health Administration, provide adequate protection for a particular pesticide or a particular use pattern, applicator exposure data may not be required for that pesticide or the use pattern. Applicants should consult with the Agency on appropriate testing before the initiation of studies.

In addressing this comment, EPA realized that this proposed language is misplaced and also needs some textual modification. As discussed previously, an OSHA PEL or

ACGIH TLV standard is part of hazard evaluation. If the PEL or TLV is determined to be adequate to fulfill EPA's selection of a toxicity endpoint, then the types and number of toxicity studies that may be required is impacted, not the need for exposure data.

Therefore, EPA has removed the language originally proposed for § 158.2260(a)(1) and § 158.2270(a)(1) concerning use of OSHA standards. With modifications, the language appears in the final toxicity rule in § 158.2230(e).

B. Poisoning Incident Data

1. *Comment.* "Poisoning incident data" should not be incorporated into this regulation unless the EPA can provide criteria to trigger the need for exposure data based on poisoning incidents. Regulating based upon anecdotal reports of "poisoning" is not appropriate.

2. *EPA's response.* Both proposed § 158.2260(b) and § 158.2270(b) contained the following trigger for requiring exposure data: "Scientifically sound epidemiological or poisoning incident data indicate that adverse health effects may have resulted from handling of the pesticide." EPA understands that anecdotal reports may or may not indicate a cause-effect relationship, i.e., that adverse health effects may or may not have resulted from exposure to the pesticide. EPA agrees that anecdotal reports may not substantiate a clear dose response relationship of "poisoning," and therefore, when not substantiated, are not appropriate for regulatory endpoints. In-depth information on the dose response is the critical information needed for regulatory endpoints, and poisoning incident data rarely include this information. However, EPA's intention was to use scientifically credible information as a trigger for requiring exposure data. Based on this comment, EPA has revised the toxicity triggers in § 158.2260 and § 158.2270 to clarify that poisoning incident data must have a clear cause-effect relationship to indicate that adverse health effects have resulted from exposure to the pesticide.

C. Use of Existing Post-Application Exposure Data

1. *Comment.* A commenter argued that there is a significant amount of post-application exposure data available that should be considered/used before requiring data under FIFRA.

2. *EPA's response.* EPA acknowledges that there are existing exposure data either in the literature, or via other governmental organizations such as OSHA, or academia, etc. When available and appropriate, EPA uses such exposure data and/or information in its risk assessments. For example, the risk assessments for both chlorine dioxide and ethylene oxide relied heavily on the workplace air concentration monitoring data available in OSHA's Chemical Exposure Health Database (CEHD), formerly known as, Integrated Management Information System (IMIS). To access CEHD, users navigate on the OSHA homepage (<http://osha.gov/>) to Chemical Exposure Health Data under the Data and Statistics section towards the bottom right of the page. Users can search CEHD by Establishment Name, State, Zip Code, Year Range, Standard Industrial Classification (SIC), North American Industrial Classification System Code (NAICS), Chemical Abstracts Service Number (CAS), Chemical Name, or Result Range.

Applicants who are aware of existing data that could fulfill a data requirement should submit the data to EPA. EPA will consider the appropriateness and robustness of the data, and, if appropriate, will use the data in the Agency's risk assessment.

D. Soil Residue and Indoor Surface Residue Dissipation Studies

1. *Comment.* A commenter claimed that there is little justification for requiring the soil residue dissipation and indoor surface residue dissipation studies.

2. *EPA's response.* In the proposed rule, EPA conditionally required the soil residue dissipation study for both occupational and residential scenarios. EPA agrees that the likelihood of requiring soil residue dissipation data is low for the majority of antimicrobial use patterns. The low likelihood is reflected in the "CR" designation in the proposed post-application exposure data requirements table for the soil residue dissipation

study for both occupational and residential use patterns. No changes are needed.

In the proposed rule, EPA required the indoor surface residue dissipation study for both occupational and residential scenarios. However, the likelihood of requiring indoor surface residue dissipation data is high for residential products such as antimicrobial-treated clothing and plastic consumer items/toys, as well as direct applications such as carpet shampoos, laundry detergents, and floor cleaners that are antimicrobial products. Therefore, the indoor surface residue dissipation study for the residential use sites will remain “R” as proposed.

However, EPA has reevaluated the “R” proposed for occupational use sites. When compared to residential use sites, occupational use sites are less likely to result in the need for indoor surface residue dissipation data. Therefore, the data requirement for indoor surface residue data has been revised from “R” to “CR” for occupational uses.

In most manufacturing settings, there is less contact with surfaces than in most residential scenarios. For example, under most circumstances workers do not crawl around the floors of manufacturing plants. The need for indoor surface residue dissipation data for workers is limited by the residue distribution where contact may occur. EPA now agrees that the occupational use sites are less likely to result in the need for indoor surface residue dissipation data, and therefore, the “R” has been revised to “CR.”

E. Non-Dietary Ingestion Study

1. *Comment.* A commenter asserted that the proposed requirement for non-dietary ingestion is impractical and unnecessary, and, in fact, could be replaced by modeling.

2. *EPA’s response.* EPA agrees that the non-dietary ingestion study is impractical, as a stand-alone direct measurement study. Non-dietary ingestion exposure (i.e., incidental oral ingestion by children) is of potential concern for treated articles or surfaces that may be accessed by children. For example, uses such as carpet shampoo, hardwood floor treatments, pressure-treated wood, and impregnated materials (including but not limited to

plastic toys or treated clothing) are assessed for non-dietary exposures when toxicity criteria are triggered. In all of these instances, non-dietary ingestion exposures are estimated using residue data from the treated surface combined with activity factors for children's behaviors (e.g., frequency of hand-to-mouth contact). Often, EPA models this route and pathway of exposure using inputs from the available and reliable published research. If EPA were to require data to estimate this exposure pathway, EPA would require surface residue data, rather than the actual monitoring of children or having individual registrants collecting data on frequency of hand-to-mouth activities, as these are not chemical-specific. Given the unlikelihood of requiring non-dietary ingestion exposure studies, EPA has determined to not finalize this proposed data requirement and its accompanying test note 12 in the final post-application exposure table in § 158.2270(e).

XIV. Environmental Fate Data Requirements

The following represent the significant comments received on the need for and evaluation of environmental fate studies as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Need for Environmental Fate Data for Indoor Uses

1. *Comment.* Several commenters argued that the proposed environmental fate data requirements for indoor uses of antimicrobials should not exceed those in part 158 for conventional pesticide chemicals, since antimicrobials are not directly broadcast into the environment.

2. *EPA's response.* As explained in the proposed rule, there is now a greater concern regarding indoor uses of antimicrobials because those antimicrobial uses can lead to environmental exposure when they go down the drain. The rationale for requiring environmental fate data for antimicrobials mirrors that of Unit XI.A. for requiring nontarget organism data for antimicrobials.

There are many uses for which a high potential for exposure exists, and these uses may require a more extensive environmental fate data set that could also include aerobic and anaerobic metabolism studies. However, such uses will typically require a much reduced first tier data set with additional testing triggered if the results of the required data indicate a potential risk that needs further characterization.

B. Transformation Products

1. *Comment.* A commenter argued that the Agency has not clearly stated when environmental fate data on the transformation products would be required. Additionally, the commenter also wanted to understand the data that would be required if the substance degrades quickly?

2. *EPA's response.* For environmental fate data, the Agency evaluates transformation products on a case-by-case basis, using several sources of information. First, the transformation products need to be identified. While product chemistry data can provide some information on degradates, environmental fate data provide data specific to a particular environmental compartment. Environmental fate studies provide information on the stability and persistence of the active ingredient and its degradation products in the various environmental media. For example, in the hydrolysis study, a half-life >30 days indicates that the substance is stable to hydrolytic processes, i.e., the substance did not degrade. Similar determinations are made based on the results of the photodegradation in soil and water studies, and the aerobic and anaerobic metabolism in soil and water studies after review of the required fate data. Monitoring and incident data, if available, also may indicate stability and persistence. There could also be environmental fate data conducted on a related chemical or information from the open literature. This analysis is critical to determining not only the need for environmental fate data for transformation products, but also is the first step for determining the need for nontarget organism or nontarget plant data for transformation products.

EPA proposed criteria to require testing of transformation/degradation products or leachate residues in proposed § 158.2280(a)(2) and (3). To respond to this comment, EPA also considered a similar comment on transformation/degradation products or leachate residues for nontarget plant and organism testing (see Unit XI.B.). In response to these comments, EPA determined to clarify and revise the criteria for testing of transformation/degradation products and leachate residues for nontarget organisms in § 158.2240(a)(3), for environmental fate in § 158.2280(a)(2), and for nontarget plant protection in § 158.2250(b).

EPA would use these criteria to determine if environmental fate data on the transformation/degradation products or leachate residues are required. Therefore, if the environmental fate studies on the parent indicate the transformation product(s) is, for example, more persistent in soils, then the same environmental fate data required for the parent are required for the transformation product(s). If concerns are identified, then higher-tiered environmental fate and/or ecological effects data on the transformation/degradation product(s) would be required.

It should be noted that the criteria for determining whether to assess risks from a chemical substance and/or its degradation products when conducting a down-the-drain analysis are different from those discussed previously. Those criteria are discussed in response to comment 130.4 in the Response to Comments Document in the docket.

C. Photodegradation in Soil Study

1. *Comment.* A commenter claimed that EPA has not sufficiently explained why a photodegradation in soil study would be required if a substance hydrolyzes and its behavior is known from its soil profile.

2. *EPA's response.* EPA proposed to require the photodegradation in soil study for only one use pattern: Wood preservatives. Wood products that have been treated with wood preservatives are often in contact with soil, and therefore it is possible for the wood

preservative chemical, as well as its transformation and degradation products, to leach out from the treated wood product. To understand the fate of wood preservative chemicals in soil, first requires an understanding of the soils properties. Soil profiles are descriptions of soil properties, both physical and chemical. Examples of physical characteristics would include: color, bulk density, and texture. Examples of chemical characteristics would include: pH of the soil, organic matter content, and Cation Exchange Capacity (CEC). Depending on the soil profile, an antimicrobial pesticide can undergo chemical and/or biochemical (biodegradation) processes. For example, if the pH of the soil is less than 7, the antimicrobial can undergo hydrolysis and become nonpersistent, or if the pH of the soil is basic, the antimicrobial could remain stable and become persistent. If the organic carbon content of a soil is high, then the soil has a high microbial population which facilitates the biodegradation process. Hence the nature of a soil (soil profile) is an important indicator of how a pesticide may behave in a soil.

Many applicants are well aware of soil profiles, since EPA asks for the soil profile to be submitted along with the results of the studies in soils. A number of soil profile data bases are available. Two of the data bases used by OPP are one from the United States Department of Agriculture (USDA) and one called CLARION.

In this final rule, EPA has retained the requirement for a photodegradation in soil study for the wood preservatives use pattern. The photodegradation in soil study is required for all wood preservatives, except for two circumstances. First, if the antimicrobial is an inorganic substance or a metal salt, then a photodegradation study does not provide applicable information for inorganics and metal salts that do not degrade (chemically or biochemically). Second, if data from standardized soil profiles show that the chemical is likely to readily degrade microbially or undergo redox reactions (degrade chemically) to such a degree that there is no formation of degradation/transformation/leachate products of concern (as defined in § 158.2280(a)(2)),

then the photodegradation in soils study would not be needed. EPA has revised the proposed test note 10 to the environmental fate table, so that test note 10 to the final environmental fate table in § 158.2280(c) explains the conditions for not requiring the photodegradation in soil study.

D. Aquatic Sediment Study

1. *Comment.* A commenter claimed that EPA is unclear about the triggers that would lead to the requirement for an aquatic sediment study, and how down-the-drain modeling could affect the need for this study.

2. *EPA's response.* Test notes 5 and 13 to the proposed environmental fate table in § 158.2280 trigger the aquatic sediment study for all use patterns except the aquatic areas use pattern. EPA has reevaluated the need for the aquatic sediment study and the appropriate triggers. EPA agrees that having two triggers, both of which use a weight-of-evidence evaluation process, is confusing, and believes that one trigger (proposed test note 13) would be sufficient for triggering the aquatic sediment study. In this final rule, EPA is removing test note 5 from the test note column for the aquatic sediment study data requirement. Based on this reevaluation, EPA also believes that the aquatic sediment study should be required for the antifoulant coatings and paints use pattern since an antifoulant use would meet the criteria of the trigger in test note 13, which is: "...data are required based on the potential for aquatic exposure and if the weight-of-evidence indicates that the active ingredient or principal transformation products are likely to have the potential for persistence, mobility, nontarget aquatic toxicity, or bioaccumulation." Antifoulants are released/applied directly to the aquatic environment. These products are often manufactured to be persistent, and because of the continuous release process, some of the active ingredient is likely to be transferred to the bottom of the water column and then be adsorbed to the sediment. This is likely to result in adverse effects on nontarget benthic organisms. Since this meets the triggers for requiring the study, in this final rule EPA is

changing the “CR” for the aquatic sediment study for the antifoulant coatings and paints use pattern to “R.”

The aquatic sediment study provides information about the degradation/dissipation processes under field conditions. The results of down-the-drain modeling are unlikely to provide appropriate information to determine the need for the aquatic sediment study. The current version of the down-the-drain model estimates concentrations of chemical substances in the water column downstream of wastewater treatment facilities, but does not estimate concentrations in the sediment.

E. Monitoring of Representative U.S. Waters Study

1. *Comment.* The commenter noted that there is no guidance on how to conduct a “monitoring of representative U.S. waters” study, and that EPA has not provided the criteria for triggering a “monitoring of representative U.S. waters” study.

2. *EPA’s response.* The commenter is correct. EPA does not have a guideline for conducting this study. For all pesticides, such monitoring (studies) of representative U.S. waters is a very rare occurrence. If EPA were to require such a monitoring study, protocols would have to be developed to specify a great deal of information:

- At which locations would the monitoring occur, and how often would the monitoring occur?
- Is the sampling for ground water, surface water, or the estuarine/marine environment?
- Which chemical substances would be monitored? Is just the antimicrobial (parent) to be analyzed, or would the transformation/degradation products also be analyzed?

Such a protocol would be specific to a particular pesticide, where that pesticide is used, and where the pesticide has been detected, and could not necessarily be used for a different pesticide.

For the monitoring of representative U.S. waters data requirement, the term “residue of concern” (ROC) is currently specified in the environmental fate data requirements table in the test substance to support column. Since the ROC would be determined during protocol development, EPA is adding this information as part of a new test note 17 to the final environmental fate table in § 158.2280.

As stated in the preamble to the proposed rule, a WOE approach would be used to determine if a monitoring of representative U.S. waters study should be required. The preamble to the proposed rule discusses this aspect in more detail (73 FR 59413). EPA expects this study to be rarely required.

F. American Wood Protection Association (AWPA) and American Society for Testing and Materials (ASTM) Methods

1. *Comment.* A commenter argued that AWP method E11-97 or E20-04, and ASTM Method D5108-90 “are of limited or no relevance to estimating environmental exposures” for wood preservatives, or antifoulants, respectively. According to the commenter, the results of the ASTM method are not suitable for “estimating release rates for regulation purposes.” The commenter believes that both methods “overestimate leach rates and are not intended for use in risk assessments.” The commenter also provided information to indicate that ASTM Method D5108-90 has been replaced by ASTM D6442-06.

2. *EPA’s response.* Test note 15 to the proposed environmental fate table in § 158.2280 triggers the special leaching data requirement for the wood preservative use pattern. EPA’s intent in specifying that it would accept an ASTM or AWP method was to allow applicants to use these readily available protocols. However, as noted in the proposed test note, protocol review was still required for some of these methods. Since the commenters believe that these AWP methods are inappropriate, but have not offered

alternative methods, test note 15 to the final environmental fate table in § 158.2280(c) is revised to remove the AWWA methods. Test note 12 to the final environmental fate table in § 158.2280(c) is added to require protocol review.

Test note 16 to the proposed environmental fate table in § 158.2280 triggers the special leaching data requirement for the antifoulant coatings and paints. Since the commenter indicated that the ASTM method has been replaced, EPA believes that specifying an ASTM method number in regulatory text may provide insufficient clarity, at some point in the future. Therefore, test note 16 to the final environmental fate table in § 158.2280 is revised to remove the ASTM methods. Test note 12 to the final environmental fate table in § 158.2280(c) is added to require protocol review.

XV. Down-the-Drain Analysis

The following represent the significant comments received on the need for and performance of a down-the-drain analysis as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Changes to Down-the-Drain Analysis Based on Comments Received

1. *Comment.* Some commenters expressed concern regarding EPA's proposal to exclude antifoulants and wood preservatives from testing designed to protect POTWs and the aquatic environment. These commenters contend that these compounds may reach POTWs through sources such as hull blast water, landfill leachate, and centralized waste treatment facilities. They think EPA should revisit this assumption to verify its accuracy.

2. *EPA's response.* Based on this comment, EPA did reevaluate its original determination to exclude antifoulant coating and paints, wood preservatives, and aquatic areas from down-the-drain analysis. EPA still believes that it is appropriate to exclude aquatic areas from a down-the-drain analysis. As discussed in the preamble to the proposed rule (73 FR 59390) aquatic areas include lakes, ponds, streams, drainage ditches,

and other bodies of water. These would not be expected to result in down-the-drain releases and are therefore unlikely to be discharged to a WWTP.

Based on its reevaluation, EPA believes that a down-the-drain analysis is needed for the wood preservative, and antifoulant paints and coatings use patterns, as well as the all other use patterns category. There are a number of sources of indirect releases of antifoulants and wood preservatives to surface water via WWTPs. The Emission Scenario Document (ESD) for Wood Preservatives, which is part of the OECD Series on Emission Scenario Documents, documents numerous sources of environmental releases directly to surface water. The ESD also describes various types of wood preservative facilities where there may be environmental releases to the facility drain that subsequently drains to a WWTP. Some of the types of wood preservative facilities identified in the OECD ESD for wood preservatives include automated spraying plants, dipping/immersion plants, and plants that employ vacuum-pressure and double vacuum processes. According to this OECD ESD for wood preservatives, it is also possible for releases to sewage treatment plants to occur from some treated wood products, such as noise barriers.

According to the OECD ESD for Antifouling Products, in addition to the numerous sources of direct environmental releases to surface water resulting from the use of antifoulant paints and coatings, there is the potential for antifoulants to enter sewage treatment plants as a result of application and removal of antifoulant paints at boatyards and marinas.

Thus, OPP's Antimicrobial Division (AD) will perform a down-the-drain assessment for every product with an applicable use or exposure scenario that has the potential for waters containing antimicrobials to reach a WWTP. To perform this assessment, the Agency is requiring data on the biodegradation of an antimicrobial pesticide and its potential toxicity to WWTP microorganisms in an activated sludge basin. For some antimicrobial pesticides, the Agency will also require the activated sludge

sorption isotherm test to determine removal from wastewater via partitioning to activated sludge. For additional information on the changes made to the proposed environmental fate data requirements table see response to comment 134.1 in the Response to Comments Document in the docket.

B. Use of E-FAST Model

1. *Comment.* According to one commenter, EPA staff indicated at the part 158, subpart W Antimicrobials Data Requirements Workshop held on November 6, 2008 that the E-FAST model may have been based on municipal WWTPs that received only “residential” discharges. The commenter suggested that is very unlikely and stated that according to the E-FAST manual, the model was based on data from actual U.S. municipal WWTPs. Nearly every municipal WWTP receives discharges from many types of non-residential sources, like commercial facilities, medical facilities, institutions, and cooling water systems (which are common in commercial buildings). Even in smaller communities, POTWs receive wastewater from residential and commercial (e.g., schools, stores, restaurants, hotels/motels, and/or medical facilities) sources. Most municipal WWTPs also receive both process and non-process discharges from industrial facilities. Some commenters contend that the E-FAST model is applicable as a screening-level model for all antimicrobial use patterns with discharges that are typically rinsed down the drain including agricultural premises and equipment, food handling/storage establishments, residential and public access premises, medical premises and equipment, industrial processes and water systems, swimming pools, and others.

2. *EPA’s response.* The E-FAST documentation manual indicates that the down-the-drain module was developed as a screening-level model for estimating concentrations of chemicals in surface water that may result from the disposal of consumer products into household wastewater. The model developers have confirmed, however, that the data base of WWTPs that is accessed by this module consists of domestic WWTPs that receive

wastewaters predominantly from residential, commercial, and institutional sources, and not solely from residential sources. In modeling releases of antimicrobial pesticides to environmental media, the appropriate data inputs, methods, and tools are dependent upon the source of the environmental releases. To assess exposures and risks to releases of antimicrobial pesticides to surface water from residential, commercial, and institutional sources, the down-the-drain module of E-FAST is the most appropriate tool.

To assess exposures and risks to antimicrobial pesticides from manufacturing, processing, and industrial use facilities, the general population and ecological exposures from the industrial releases module of E-FAST is the most appropriate tool. The decision to use the general population and ecological exposures from the industrial releases module is made on a case-by-case basis considering the availability of data required as inputs to the module, and the potential for significant exposure. For example, a low volume use may not require use of this module.

EPA agrees that the E-FAST model is applicable as a screening-level model for all antimicrobial use patterns with discharges that are typically rinsed down the drain, including agricultural premises and equipment, food handling/storage establishments, residential and public access premises, medical premises and equipment, industrial processes and water systems, swimming pools, and others.

C. Exceedance Levels

1. *Comment.* Some commenters questioned the justification for the following exceedance levels that were used by EPA to evaluate potential risks to aquatic organisms:

i. Potential risks from effects to aquatic invertebrates and fish: Exceedance of the chronic concentration of concern (COC) for 20 or more days triggers a potential for concern;

ii. Potential risks from effects to aquatic invertebrates and fish: Exceedance of the acute COC for 4 or more days triggers a potential for concern; and

iii. Potential risks from effects to algae: Exceedance of the COC for algae for 4 days or less may trigger a concern and is evaluated on a case-by-case basis.

2. *EPA's response.* Exceedance levels and corresponding number of days of exceedance that trigger potential for concern are those cited in EPA/OPPTS/OPPT's "Interpretive Assistance for Sustainable Futures Summary Assessment", last updated August, 2011. The justification that the potential for chronic risk to aquatic organisms may exist if the predicted environmental concentration (PEC) exceeds the chronic COC and the exceedance occurs for 20 days or more per year is documented on page 11:

The potential for chronic risk to aquatic organisms may exist ONLY if the PEC exceeds the chronic COC for 20 days or more per year. If exposure occurs for 20 days or more per year, the concentration of the chemical in surface water may reach levels associated with chronic effects (Lynch et al., 1994). The 20-day criterion is derived from partial life-cycle tests (Daphnid chronic and fish early life-stage tests) that typically range from 21 to 29 days in duration. Low concentration for chronic risk exists if the COC is exceeded on fewer than 20 days per year.

The justification for the potential for acute risks to aquatic organisms appears on page 12:

The potential for acute risk to aquatic organisms exists if the predicted environmental concentration (PEC) is greater than the acute concentration of concern (COC).

If Acute COC > PEC: Low concern for risk

If Acute COC < PEC: Potential for risk

EPA notes that risk is influenced by both the duration of exposure and the likelihood of that exposure occurring. Often mathematical models are used to estimate exposures and risks. There are two types of models: Deterministic or probabilistic. Probabilistic modeling is a technique that utilizes the entire range of input data to develop a probability distribution of risk or exposure rather than a single point value. The analysis identifies the probability that the exposure exceeds the COC and for what timeframe. Deterministic modeling is based on select input data that result in a single point estimate. The estimate either exceeds or does not exceed the COC. Models such as E-FAST have the capability of providing either deterministic or probabilistic results. Consequently, criteria for determining whether or not testing on aquatic organisms is required need to take into account the possibility that the estimated exposure could be modeled using either deterministic or probabilistic modeling. Therefore, two test notes to the final nontarget organism table in § 158.2240 have been revised to include a probabilistic trigger for down-the-drain analyses, while retaining the existing deterministic trigger for releases of antimicrobials that are expected to enter WWTPs. Test note 7 to the final nontarget organism table in § 158.2240(c) triggers the acute freshwater invertebrate toxicity study (TEP testing) and the acute freshwater fish toxicity study (TEP testing). Test note 12 to the final nontarget organism table in § 158.2240(c) triggers the fish life-cycle study.

D. Evaluation of Discharges to Still Water and to Salt Water

1. *Comment.* During the Antimicrobial Data Requirements Workshop held on November 6, 2008, EPA staff indicated that evaluation of discharges to still water and to salt water would be challenging. The commenter argued that the E-FAST model manual suggests that these discharges can be readily evaluated with appropriate input data and elimination of the PDM (Probabilistic Dilution Model) option.

2. *EPA's response.* EPA believes that the commenter misunderstood the context of the Information provided by EPA staff both in the proposed rule and at the presentation

on November 6, 2008. E-FAST has two modules for estimating releases to surface water: The down-the-drain module, and the general population and ecological exposure from industrial releases module.

When the down-the-drain module of E-FAST is run without the PDM option, the results are limited to estimates of concentrations in surface water downstream of domestic wastewater treatment facilities. The down-the-drain module has no option for estimating concentrations in non-flowing waterbodies such as lakes, bays, estuaries, and oceans. The discussion at the November 6, 2008, Workshop focused solely on the down-the-drain module.

E-FAST, however, has the capability for evaluating discharges to still water and to salt water from discharges to WWTPs that receive manufacturing, processing, and industrial use releases, but not from discharges to surface water via domestic WWTPs. The general population and ecological exposure from industrial releases module is designed to estimate releases to air, water, and land from manufacturing, processing, and industrial use of chemical substances. The data base for estimating releases to WWTPs that primarily receive wastewater from manufacturing, processing, and industrial uses requires estimates of releases to environmental media from models such as ChemSTEER (Chemical Screening Tool for Exposures and Environmental Releases), a model developed by EPA's OPPT or from data and calculations included in standard scenarios, also developed by OPPT (www.epa.gov/oppt/exposure/pubs/chemsteerdl.htm). The general population and ecological exposure from industrial releases module includes an option for estimating concentrations in lakes, bays, estuaries, and oceans.

E. Parameters for Down-the-Drain Analysis

1. *Comment.* Several commenter's argued that EPA's approach for down-the-drain chemicals separates the exposure and the effects of the assessment and subjects chemicals to similar testing requirements regardless of the mass of chemicals disposed of

in the environment. According to these commenters, the fact that EPA does not guide testing by the extent of environmental exposure is wasteful for ingredients which will reach the environment at low levels. Even for chemicals which are used at greater volume, the commenters claimed that there is no proof that EPA's program will achieve its goal without being wasteful and some commenters believe that EPA's approach will likely result in significant unwarranted costs in animals, time, and dollars. The commenters asserted that this will result in unnecessary loss of animals, increased costs to the consumer and will negatively affect product innovation as new product development will be slowed due to the extra regulatory burden. The benefit to the environment of the EPA approach, according to the commenters, is likely to be small and not commensurate with its costs.

2. *EPA's response.* EPA disagrees with this comment. Three key input parameters for the down-the-drain model are:

- i. Percent removal of antimicrobial pesticide during wastewater treatment;
- ii. Concentrations of concern for antimicrobial pesticides based on acute and chronic end-points for freshwater fish, freshwater invertebrates, and freshwater plants; and
- iii. Wastewater treatment plant influent volume of antimicrobial pesticide.

As demonstrated in the sensitivity analysis of the down-the-drain model in the document, "Four Case Studies of Antimicrobial Pesticides in the Down-the-Drain Screening Model, Using the Proposed Approach for a Screening-Level Environmental Fate Assessment" (identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0044), the amount of chemical disposed in the environment strongly influences the results of the down-the-drain model. It is possible that if the amount of chemical disposed is small (i.e., WWTP influent volume is low and/or high percent removal during wastewater treatment), the predicted surface water concentration of the antimicrobial, even for a chemical of high toxicity, would not exceed the Agency's level of concern. Under such circumstances, higher-tier testing (environmental fate, ecotoxicity, and plant protection) is

unlikely to be triggered. Since higher-tier testing is triggered only if the down-the-drain model indicates that the predicted concentration of the antimicrobial may adversely affect aquatic organisms this reduces the number of tests required, and therefore the animals, time, and dollars.

EPA also notes that two of the three key input parameters needed to run the down-the-drain model, percent removal during wastewater treatment and wastewater treatment plant influent volume do not involve animal testing and would not lead to loss of animals. Fate tests required to determine removal during wastewater treatment via biodegradation and adsorption are inexpensive. No costs are associated with WWTP influent volume.

F. Acute and Chronic Toxicity Endpoints

1. *Comment.* At the Antimicrobial Data Requirements Workshop held on November 6, 2008, EPA staff indicated that chronic aquatic toxicity endpoints might not be used to evaluate antimicrobial discharges from municipal WWTPs. A commenter argued that since EPA/OW requires municipal WWTPs to conduct both acute and chronic toxicity tests regularly as conditions of CWA-regulated National Pollution Discharge Elimination System (NPDES) permits, both acute and chronic endpoints should be evaluated by EPA/OPP to ensure that antimicrobial discharges will not cause toxicity in municipal WWTP effluent.

2. *EPA's response.* To assess whether the proposed screening level assessment and tiered system of data requirements provides the data needed to assess exposure and risk of antimicrobial pesticides released to the environment via down-the-drain use patterns, the Agency conducted four case studies (73 FR 59408-9). Based on this comment, EPA has reevaluated the approach used for the case studies, in which the higher-tiered data was triggered based on the results of the available data. To ensure that antimicrobial discharges will not cause toxicity to aquatic organisms downstream of WWTP effluents requires an evaluation of both acute and chronic toxicity endpoints. This

means that the chronic ecotoxicity data needs to be submitted at the same time as the acute ecotoxicity data, so both types of studies are available for EPA to use for the ecological risk assessment. Also see Units XV.A. and B.

Consequently, in the final nontarget organism table in § 158.2240(c), the table descriptors for the fish early-life stage and aquatic invertebrate life-cycle tests have been changed from “CR” to “R” for the wood preservatives use pattern and the all other use patterns category. Test note 10 to the final nontarget organism table in § 158.2240(c) has been modified to remove the trigger since it is no longer needed.

XVI. Residue Chemistry Data Requirements

The following represent the significant comments received on the need for and evaluation of residue chemistry studies as proposed by EPA. Changes from the proposed rule to the final rule are also described. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Scope of the Residue Chemistry Data Requirements

1. *Comment.* Several commenters found the scope of coverage of the residue chemistry data requirements in § 158.2290(b) to be vague and confusing. Further, the ACC Biocides Panel asserted that this section required data for uses for which a FFDCA section 408 tolerance is not required and over which, therefore, EPA allegedly has no jurisdiction.

2. *EPA's response.* EPA is clarifying § 158.2290(b) which pertains to the scope of the residue chemistry data requirements. That section can be read as limiting the residue chemistry data requirements to pesticide products requiring a tolerance or tolerance exemption. This apparent limitation is inconsistent with both the preamble's general description of the scope of subpart W and the preamble's description of the scope of the residue chemistry data requirements section, and is internally inconsistent with the terms of § 158.2290(b). Various commentators noted the lack of clarity in this portion of the rule.

The preamble’s general discussion of the scope of subpart W made clear that this subpart was not limited to “antimicrobial pesticides” as defined by FIFRA section 2(mm) – which excluded antimicrobial pesticide uses subject to either FFDCA section 408 or section 409 – but extended to among other things, “[p]esticide products for antimicrobial use in/on food” (73 FR 59385). In no way, however, did this discussion suggest or imply that the subpart is limited to antimicrobial uses requiring FFDCA section 408 tolerances or exemptions from tolerances. To the contrary, the preamble’s discussion of toxicity data requirements expressly notes that data are needed under subpart W to assess dietary risk whether or not a section 408 tolerance is required. The preamble specifically states that, although certain antimicrobial food uses are regulated under the FFDCA by FDA under section 409 and not section 408, EPA still needs data on these uses to assess dietary risk to fulfill its statutory obligations under FIFRA section 2(bb)(2), which establishes the FFDCA section 408 safety standard as a component of the FIFRA standard for registration/cancellation for FIFRA pesticide uses that result in residues on food (73 FR 59394). Further, the preamble’s discussion of residue chemistry data requirements states that these data are needed for “direct and indirect food uses” including application to “food or water” both to assess risk and for tolerance-setting purposes (73 FR 59401: “In addition to dietary risk assessments, residue chemistry data are used to establish pesticide tolerance”). Finally, both the preamble’s discussion of residue data requirements and the relevant rule text mention antimicrobial uses that would be excluded by a limitation of the rule to antimicrobial uses requiring tolerances. For example, both the preamble and rule text refer to “fruit and vegetable rinses,” antimicrobials “incorporated into a material that may contact food or feed,” and “[a]quatic uses that have the potential to result in residues in potable water” and the fact that all of these uses may not need section 408 tolerances (73 FR 59401 and 59444).

Accordingly, EPA is revising § 158.2290(b) to make clear it is not limited to

antimicrobial uses which need FFDCA section 408 tolerances. With some modifications, EPA is retaining in § 158.2290(b) a non-exclusive list identifying examples of antimicrobial products covered by this section. The revision to the introductory text of § 158.2290(b)(1) makes clear that the residue data requirements apply to antimicrobial products that may result in residues in food or water whether or not a FFDCA section 408 tolerance is needed.

The first item in the list of covered uses now reads “Products that require a tolerance, tolerance exemption, or food additive regulation or clearance.” The insertion of the reference to food additive regulations and clearances is consistent with the rule’s scope which is not limited to pesticide uses regulated under FFDCA section 408. Additionally, each of the subparagraphs listing examples of covered uses has been revised to refer to “products” rather than “uses” for consistency and clarity. Although the subparagraphs are overlapping (i.e., a product may fall in more than one paragraph), the revised subsection now clarifies the overall scope of the section. These revisions make § 158.2290(b) consistent with the scope of the rule described in the preamble and the scope of the toxicology data requirements.

Not only are these changes consistent with the scope of the rule as discussed in the preamble (i.e., data requirements are not limited to uses needing section 408 tolerances) but the revised language’s focus on whether use of a pesticide may result in residues in or on food follows directly from the intent of the residue chemistry requirements as discussed in the preamble. There, EPA explained that the proposed requirements will provide information “to better estimate human dietary exposure to antimicrobial residues in or on food or feed,” “to determine the composition of the pesticide residue and how much of the residue is present in food or animal feed,” and to “measure how much of the residue of concern is present in food, feed, and water” (73 FR 59401). Further, the revised language is consistent with the scope of FFDCA section 408 (applies to “pesticide chemical

residue[s] in or on food”) and FIFRA (requires consideration of “residues that result from the use of a pesticide in or on food”). It also follows directly from the existing data requirements applying to antimicrobials in part 161. Those regulations provide that “Residue Chemistry Data are used by the Agency to estimate the exposure of the general population to pesticide residues in food and for setting and enforcing tolerances for pesticide residues in food or feed.” 40 CFR 161.202(c)(1); *see also* 40 CFR 161.202(c)(2) (“results of tests on the amount of residues remaining on or in the treated food or feed are needed to support a finding as to the magnitude and identity of residues which result in food or animal feed as a consequence of a proposed pesticide usage”); 40 CFR 161.240(b)(14) (Residue data on indoor use of pesticide “if such a use could result in residues in food or feed”). Finally, the revised language also tracks EPA’s requirements for residue chemistry data under the current data requirements for conventional pesticides in 40 CFR part 158, subpart O. In the preamble to the proposed rule, EPA explained that the residue data requirements for antimicrobials were adapted from the conventional data requirements in subpart O (73 FR 59401). For uses of conventional pesticides, other than uses in agriculture, part 158 states that “[residue chemistry] [d]ata may be required . . . if residues may occur in food or feed as a result of the use.” (40 CFR 158.1410(b)(2)). The regulation also makes clear that this requirement applies whether or not a tolerance is needed under FFDCA section 408. The regulation specifies that “most products used in or near kitchens require residue data for risk assessment purposes even though tolerances may not be necessary in all cases.” (Id.)

The commenters’ concern that the residue chemistry requirements exceeded EPA’s jurisdiction under the FFDCA is addressed in Unit IV.

B. Complete Transference of the Antimicrobial into Food

1. *Comment.* The commenter believes that additional clarification is needed concerning EPA’s statement, “in the absence of data [the Agency will] evaluate the need

for a tolerance or tolerance exemption by assuming complete transference of the chemical into food over the lifetime of the treated product.”

2. *EPA’s response.* Complete transference refers to an assumption that the Agency would initially make regarding the migration of antimicrobial residues from an impregnated food contact material to the food contacting that material over the typical use life of the antimicrobial-impregnated material. The worst-case assumption is that 100 percent of the antimicrobial residues resulting from use at the maximum registered rate transfers into the food, which is then used to estimate a conservative dietary exposure. If the aggregate risk calculated using this conservative assumption, from use of the antimicrobial in question, is less than EPA’s level of concern, then no measured data are needed. If the aggregate risk meets or exceeds EPA’s level of concern, then chemical-specific data quantifying residue migration to refine this dietary exposure component may be required. To refine the exposure, the applicant may choose to perform one or more of the FDA protocols to estimate migration rate into food stimulants (see document ID number EPA-HQ-OPP-2008-0110-0013). Alternatively, or subsequently, the applicant may choose to conduct a chemical-specific nature of the residue on surfaces study and a migration study investigating actual impregnated materials using representative foods.

C. Alternative Formats for Residue Chemistry Data Requirements Table

1. *Comment.* Two different commenters suggested two different options as alternative approaches to the antimicrobial residue chemistry data requirement table proposed by EPA. One of the commenters separated the residue chemistry data requirements into two tables, referred to as Part 1 and 2 (ACC comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0088.10, p. 7). The other commenter suggested a single table format (CSPA Comment, identified in the docket by document ID number EPA-HQ-OPP-2008-0110-0086.2).

2. *EPA’s response.* All three of the commenter-suggested tables had the same five

“Supporting Information” studies as the first section of the table proposed by EPA, but with various mixtures of “R,” “CR,” and “NR.” In the final rule, EPA has retained the same Supporting Information of the first section of the residue chemistry table as proposed. However, EPA has adopted the commenters’ suggestion for a tiered format in the last two sections of the residue chemistry table. After review, EPA believes the commenters’ suggested tiered approach is more suitable to antimicrobials than that proposed by EPA. All three of the commenters’ tables suggested that Tier I consist of a “Screening-level dietary exposure assessment.” Although an applicant may opt to conduct a dietary exposure assessment, EPA does not consider this to be a data requirement. Applicants often conduct a dietary exposure assessment to understand the dietary risks before submitting an application to EPA. If submitted, EPA would review the assumptions used by the applicant and compare them to EPA’s modeling. If the applicant’s modeling indicates that dietary risk is likely to meet or exceed the Agency’s level(s) of concern, the applicant may decide to continue on to Tier II or III. Therefore, EPA has not added a requirement to conduct a dietary exposure assessment.

Both the Part 1 Table and the single table suggested that Tier II consist of a “Refined dietary exposure assessment.” As is the case for the commenter’s suggested Tier I “Screening-level dietary exposure assessment,” this is optional for the applicant; therefore, EPA has not added a requirement to conduct a refined dietary exposure assessment.

Both the Part 1 Table and the single table suggested that Tier 3 consist of nature of residue on surface, bioaccumulation, magnitude of residue, residue analytical method, and storage stability. These are each addressed individually as follows:

- i. *Nature of residue on surface.* The Agency agrees that this study is applicable and a valuable addition to the data set necessary to support registration and risk assessment of antimicrobial uses on/in food-contact surfaces and impregnated materials (treated articles).

EPA has added this study to the final residue chemistry data requirements table in part 158, subpart W.

ii. *Bioaccumulation*. EPA believes that the commenters intended that this study apply only to fish and that the bioaccumulation study required for ecological effects should substitute for the nature of the residue on surface study for aquatic uses or indoor/outdoor raw agricultural commodity uses. EPA has found that the fish bioaccumulation study is often not useful for residue chemistry purposes because characterization of fish residues is only required if the bioconcentration (of total residues) factor is $> 1,000$. The fish bioaccumulation study has not been adopted by EPA for residue chemistry. Of much more use to residue chemistry and retained in this final rule, are the fish metabolism and magnitude of the residue studies in fish described in OPPTS Guideline 860.1400.

iii. *Magnitude of residue (MOR)*. Commenters proposed this study by the very general title “Magnitude of residue.” EPA considers MOR to be any study designed to quantify “how much” of the residues of concern will result in food, on surfaces, in water, etc., following use of an antimicrobial according to label directions. The commenters stated in a footnote to this study that, in the case of food-contact sanitizers and treated articles, MOR would consist of a migration study. Because food-contact sanitizer and treated article uses comprise at least 80 percent of all antimicrobial food uses, EPA has retained the migration study and the food-handling study by name but has moved them to a different tier. All the remaining proposed types of MOR studies are much more rarely required due to characteristics such as the use pattern and/or physicochemical properties of the antimicrobial in question. For that reason, the following have been grouped as “Higher tiered” studies in the final rule: Nature of the residue in plants, nature of the residue in livestock, residue analytical methods for tolerance enforcement, multiresidue method testing, potable water, fish, irrigated crops, meat/milk/poultry/eggs, crop field trials, processed food or feed, and anticipated residues.

iv. *Residue analytical method.* EPA agrees with the commenters that an analytical method for data collection is required whenever magnitude of the residue studies are required. The Agency has retained this study in the final Residue Chemistry Table.

v. *Storage stability.* EPA agrees with the commenters that storage stability data are required whenever magnitude of the residue studies are required. The Agency has retained this study in the final Residue Chemistry Table.

The Part 2 Table did not recommend requiring a Refined Dietary Exposure Assessment. Rather, its Tier 2 consists of studies entitled nature of the residue in commodity, nature of the residue in livestock, residue analytical methods for enforcement of tolerances, multiresidue analytical method, magnitude of the residue: in commodities, in water, and in meat/milk/poultry/eggs, storage stability, and anticipated residues. EPA agrees that all of these studies should be required and has retained all of them in the highest tier in the final Residue Chemistry Table. Note that two of the commenter-suggested studies (nature of the residue in commodity and magnitude of the residue in commodities) were considered applicable only to raw agricultural commodities (RACs) treated via a fruit and vegetable rinse; whereas, the analogous EPA data requirements apply to both crop plants and metabolically-active RACs. The data requirements in EPA's final rule easily subsume the studies suggested by a commenter in Part 2. The commenters feel that EPA only has authority to require residue data for RACs of plants treated by a fruit or vegetable rinse whereas EPA interprets FIFRA and FFDCA, as amended by FQPA, to mean that data may be required for any use if necessary to support registration of any use under FIFRA (see Units XVI.A. and IV.).

As evidenced by the recommendation to divide EPA's single proposed data requirement table into two tables (Parts 1 and 2), the commenters believe the data requirements are distinctly different depending on the use pattern of interest. While this is sometimes the case, the Agency has found that there is much overlap between which

studies are necessary to characterize the dietary exposure potentially resulting from a given use. This is why the test notes provide the conditions under which each study is required, likely to be required, or not required. EPA has historically used and currently uses a single data requirement table for each scientific discipline; doing so permits the interrelationships between use pattern, tiering, and data needs to be fully evident.

The commenters did not account for data needed to estimate dietary exposure associated with uses that do not require a FFDCA section 408 tolerance or exemption (see Unit XVI.A. and Unit IV.). The commenters also did not account for data needed to estimate dietary exposure from food residues inadvertently resulting from, but not limited to, discharges of antimicrobial-treated water from indoor industries, leaching from preserved lumber, or treatment of food crops when a public health claim is made on the label.

XVII. SAR and QSAR, and the OCSPP (formerly OPPTS) Integrated Testing Vision

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Guidance on Policies, Procedures, and Processes

1. *Comment.* A commenter asked EPA to provide clear guidance on its policies, procedures, and processes on the use of alternative technologies such as SAR and QSAR, and the WOE approach. In addition, the commenter stated that EPA should also provide education and training on these approaches.

2. *EPA's response.* The Agency encourages applicants to create submissions that include predictive techniques such as SAR and QSAR to fulfill data requirements. As described in the white paper to the proposed rule, entitled, "Use of Structure-Activity Relationship (SAR) Information and Quantitative SAR (QSAR) Modeling For Fulfilling Data Requirements for Antimicrobial Pesticide Chemicals and Informing EPA's Risk

Management Process” (see document ID number EPA-HQ-OPP-2008-0110-0045), an important part of the applicant’s submission is the rationale. The rationale, or WOE evaluation, is the part of the submission that explains the applicant’s belief as to why and how the predictive data would fulfill the data requirement. The WOE approach requires a critical analysis of the entire body of available data for consistency and biological plausibility. In support of a request that predictive data be considered, the applicant would need to explain why it believes the surrogate data or the modeling are appropriate for the intended use and are of sufficient completeness and quality, and therefore would fulfill the data requirement. The Agency would evaluate each submission with a WOE rationale on a case-by-case basis.

The general types of information that are considered appropriate for a WOE approach would include:

- *Sufficiency of data.* Studies that completely characterize both the effects and exposure of the agent have more credibility and support than studies that contain data gaps.
- *Quality of the data.* Potentially relevant studies are judged for quality and studies of high quality are given more weight than those of lower quality.
- *Evidence of causality.* The degree of correlation between the presence of an agent and some adverse effect is an important consideration.

Regarding SAR/QSAR, the white paper to the proposed rule (p. 30) discusses the five criteria set by the OECD for evaluating a model. EPA encourages submitters to follow the established criteria set by OECD, and show how the model is validated for that particular pesticide chemical structure as a measure of the model’s applicability.

Different computer software programs are used to estimate/predict different hazards (see: <http://www.epa.gov/oppt/sf/tools/methods.htm>). This means that predictive software models for different scientific disciplines are not at the same level of development. The Agency has long standing experience in predicting (modeling)

physical-chemical properties, environmental fate, ecotoxicity, and experience in predicting carcinogenesis for certain classes of chemicals. However, the Agency is still gaining experience to become familiar with predictive approaches that look at other human health endpoints (e.g., reproductive, developmental), which have not been widely used at EPA. Given the different stages of predictive software development, EPA would expect to undertake a case-by-case evaluation of submitted WOE. EPA encourages the use of integrated approaches that combine the knowledge from existing data bases about the chemical of interest with data from appropriate surrogate chemicals.

EPA agrees that guidance on the policies, procedures, and processes for using alternative approaches such as SAR/QSAR is needed. In developing such a guidance document for pesticides, EPA sought to harmonize its approach with that of Canada's PMRA . The guidance document was issued as a North American Free Trade Agreement guidance document in 2012. This guidance document adheres to the five OECD principles that were discussed in the white paper and is now considered to be the definitive source of information for applicants seeking to use SAR and QSAR approaches for fulfilling data requirements for pesticide registration. For information, see

<http://www.epa.gov/oppfead1/international/naftatwg/guidance/guidance.htm>.

B. Integrating SAR/QSAR Within the Data Requirements Rule

1. *Comments.* One commenter argued that there should be an explicit statement that SAR and QSAR can be considered to fulfill data requirements. Another commenter had concerns on codifying the use of SAR in 40 CFR part 158, subpart A since that would mean that "SAR/QSAR Techniques would be applicable to conventional, biochemical and microbial, and antimicrobials pesticide chemicals." Another commenter requested that SAR/QSAR be fully integrated within the rule.

2. *EPA's response.* EPA has and will continue to consider accepting SAR/QSAR to fulfill its data requirements on a case-by-case basis. Acceptance would be based on the

information provided and most especially on the supporting rationale submitted to EPA. The Agency would evaluate the information submitted to determine if the applicant has provided information that is of sufficient quality and completeness. The Agency notes that validation of QSAR models is necessary before the predictions from those models can be fully integrated into the testing requirements. To that end, QSAR models must be inclusive of pesticide toxicology data and chemical structures. Until these models become customized with pesticide information, full incorporation of predictive tools likely will be limited to a case-by-case basis.

EPA agrees that if use of SAR/QSAR were to be codified in subpart A, that it would be applicable to all pesticide chemicals. At this time, EPA is not codifying the use of SAR and QSAR in subpart A.

XVIII. Guidelines

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Commenters' Concerns with Guidelines

1. *Comment.* Several commenters indicated their belief that the current Harmonized Guidelines have significant problems, which include:

- Lack of guidelines could create an unevenness from one company to another in how the data requirements are applied.

- Data requirements for which guidelines are not available.

- Older, outdated guidelines that need revision.

- Draft guidelines that need to be finalized.

- Older exposure guidelines that do not include information about the Human Studies Review Board.

- Guidelines that were adopted without the opportunity for public comment.

According to the commenters, lack of current guidelines could create an unevenness from one company to another in how the data requirements are applied. The commenter argued that the Agency needs to provide current, consistent, and reliable guidance and standards for each data requirement. The commenters recommended that EPA finalize all of its guidelines before the final rule is published per the recommendation from OMB.

2. *EPA's response.* EPA's Harmonized Test Guidelines are publicly-available at <http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm>. The Harmonized Guidelines contain recommendations on how to conduct a study that is most likely to provide the information needed by EPA for making a registration decision.

The Harmonized Guidelines are guidance. The guidelines themselves do not impose mandatory requirements. Applicants are not required to submit studies developed according to the guidelines to fulfill a data requirement. However, EPA encourages applicants to use the guidelines. These guidelines were developed to provide applicants, who would be conducting the studies, with recognized approaches for developing high quality data, guidance on evaluating and reporting data, definition of terms, and suggested study protocols. It would not be possible to address every conceivable circumstance that could occur when conducting a particular study. Instead the guidelines provide a framework that provides recommended approaches for conducting studies while offering flexibility and accommodation for individual circumstances where appropriate. EPA has reviewed and accepted many studies, on a case-by-case basis, that were not conducted in accordance with current guidelines, but which provided suitable information for risk assessment purposes.

Since guidelines cannot account for every conceivable circumstance, EPA, for certain studies, proposed a "required" or "highly suggested" protocol submission and review step in the test notes to the tables in the proposed rule. Generally, these pertain to

those studies that are “newer” or have not been routinely conducted. Given that the applicant community and contracting laboratories would have less experience in conducting these kinds of “newer” studies, protocol submission, review, and meetings about proposed protocols are beneficial to both the applicant and EPA, and help assure that the study submitted for review should provide the information needed by EPA for its registration decision.

EPA acknowledges that in some instances there are: Data requirements for which guidelines are not available; outdated guidelines that need revision; and draft guidelines that need to be finalized. Ideally, up-to-date final guidelines would be available for every data requirement. Up-to-date guidelines increase the possibility that EPA will receive useful data and that applicants can produce such data in the most cost-efficient and consistent manner. However, given the rapidly evolving scientific methods for conducting toxicity, exposure, and ecological studies with pesticides, study guidelines often need frequent updating to include the latest techniques and methods. Moreover, the need for openness and transparency means that developing a guideline or updating an existing one can be a lengthy process. In a letter to CropLife America (June 26, 2009), (Ref. 12) the Agency discussed the timeframe for developing the Terrestrial Field Dissipation Guideline (835.6100), which spanned 15 years. During that time period, there were presentations to the SAP, at various symposia, including ones conducted by the American Chemical Society and the American Society of Agronomy, and to a workshop in Washington, DC co-hosted by EPA and Canada’s Pest Management Regulatory Agency.

Thus, the reality is that test guidelines will always be a work in progress. At the same time, EPA is implementing a regulatory program under FIFRA and FFDCA section 408 under which it must make timely decisions on the safety of pesticide products based on toxicity and exposure testing. Guidance on optimal testing procedures remains an Agency goal but the absence of testing guidelines is not a barrier to the imposition of

testing requirements necessary to make the required statutory findings.

In 2008, OMB, during its Executive Order 12866 review of the proposed rule, recommended that certain draft guidelines be finalized before publishing the Antimicrobial Data Requirements final rule. These guidelines were:

- Applicator product use information (OPPTS 875.1700).
- Post application product use information (OPPTS 875.2700).
- Indoor surface residue dissipation (OPPTS 875.2300).
- Non-dietary ingestion (OPPTS 875.3000).

In the proposed rule (73 FR 59382, October 8, 2008), EPA discussed that the publicly-available versions of these draft guidelines were available on the SAP portion of EPA's website <http://www.epa.gov/scipoly/sap/meetings/1998/march/contents.htm>. Since the two product use information related guidelines (875.1700 and 875.2700) are expected to provide similar guidance for the narrative descriptions that the related data requirements call for, EPA intends to update them together.

The indoor surface residue dissipation draft guideline (875.2300) will be updated before issued in final form to account for new advances in how exposure is measured and modeled and to provide more information on additional methods. EPA intends to revise the draft guideline to expand the methods for antimicrobial uses, and has begun to work with EPA's ORD to develop additional methods (e.g., one current project is to develop guidance for testing in small scale air chambers). EPA is also consulting with the Consumer Product Safety Commission (CPSC) to review their sampling methods for similar products (e.g., chemicals leaching from fabrics).

Also, as previously discussed, the proposed data requirement referencing the non-dietary ingestion guideline (identified as 875.3000) is not included in the final post-applicator exposure table in § 158.2270. As a result, that draft guideline is no longer referenced in part 158. (See Unit XIII.D.).

In addition, as noted in the proposed rule, EPA notes that it has reviewed and accepted many studies, on a case-by-case basis, that were not conducted in accordance with current final guidelines, but which serve its needs and provide suitable information for risk assessment purposes. The guidelines themselves do not impose mandatory requirements. Instead, they present recognized standards for conducting acceptable tests, guidance on evaluating and reporting data, definition of terms, and suggested study protocols. The draft guidelines, therefore, serve as a starting point for developing study protocols. The Agency's scientists can also provide guidance to applicants, registrants, or task forces on aspects of study design that is often discussed at pre-protocol submission meetings. The Agency's scientists are always willing to work with individual applicants or registrants to develop study designs to fulfill data requirements.

EPA acknowledges that the guidelines for dermal and inhalation exposure studies need revisions to account for new advances in how exposure is measured and modeled. To provide needed information to the public and applicants, EPA will change the way these guidelines are referenced on the Harmonized Guidelines website by adding links to the SAP and Human Studies Review Board (HSRB) meetings at which the changes needed to conduct one of these studies were publicly discussed.

Since the publication of the proposed rule on October 8, 2008, EPA has worked to update and finalize a number of guidelines. In the **Federal Register** of April 15, 2009 (74 FR 17479) (FRL-8352-8), EPA issued a Notice of Availability describing updates to 16 environmental fate guidelines.

In the **Federal Register** of January 27, 2010 (75 FR 4380) (FRL-8437-2), EPA published four draft product performance guidelines for comment (i.e., 810.2000, 810.2100, 810.2200, and 810.2300). These four guidelines were developed over an extended period of time with multiple levels of review across divisions and program offices in EPA, expert external peer review by the FIFRA SAP, and discussions with and

comments from the regulated community. After soliciting public comment in 2010, EPA announced the availability of the final guidelines in the **Federal Register** of March 16, 2012 (77 FR 15750) (FRL-9332-4). Many of the technical changes described in these four guidelines have been in use by the Agency for several years.

Three additional Product Performance Guidelines (i.e., 810.2400, 810.2500, and 810.2600) published for public comment on September 15, 2011 (76 FR 57031) (FRL-8879-1), and in the **Federal Register** of June 27, 2012 (77 FR 38280) (FRL-9349-5), EPA announced the availability of the final guidelines.

Also in the **Federal Register** of June 27, 2012 (77 FR 38282) (FRL-9333-1), EPA announced the availability of 26 Ecological Effects Test Guidelines in Series 850, and Groups B, C, D and F. In finalizing the guidelines, EPA changed the numbering and/or titles of certain guidelines, and split or merged other guidelines. EPA continues to work to revise the remaining Ecological Effects Test Guidelines, Group A, and anticipates finalizing many of these guidelines in 2013.

Before finalizing a guideline, EPA provides many opportunities for public comment. EPA's commitment to transparency is not new. Transparency allows all stakeholders to know what, how, and why EPA is adopting a guideline. EPA's procedures for developing a guideline is described in a Notice of Availability that published on August 28, 1996 (61 FR 44308) (FRL-5390-7):

- Guidelines under development (whether new or being substantially revised) are made available for public comment.
- Guidelines under development (whether new or being substantially revised) undergo an external peer review process. Most commonly, the peer review process would be a review by the FIFRA SAP.
- Reformatted guidelines (no substantial revisions) are not subject to review and comment.

- Public review and comment is also used when EPA guidelines are being harmonized with OECD guidelines.

B. Harmonization of Guidelines with OECD

1. *Comment.* EPA should harmonize its guidelines with those of OECD.

2. *EPA's response.* EPA agrees with this comment and is continuing to harmonize guidelines, to the extent practicable, as they are revised. As noted on its website <http://www.epa.gov/pesticides/science/guidelines.htm>, EPA has several harmonization activities underway with the OECD. The Master List of Harmonized Test Guidelines includes a reference to an OECD guideline, once harmonized. All harmonized OECD test guidelines (<http://www.epa.gov/epahome/exitepa.htm>) fall under the OECD Mutual Acceptance of Data decision, which calls for acceptance for regulatory use by all OECD member nations. Additionally, under 40 CFR 158.70(d)(2), acceptance of testing conducted in accordance with OECD protocols is described.

Harmonized test guidelines reduce the burden on chemical producers and conserve scientific resources, including the minimal use of laboratory test animals. They also form a basis for work sharing and cooperation among all OECD countries. U.S. experts are engaged in harmonization activities through OECD to revise toxicology and ecotoxicology test guidelines. These revisions will emphasize reduction, refinement, or replacement of animal testing, while incorporating the latest advances in science. Animal welfare concerns and international regulatory needs are being considered in the course of these revisions of the test guidelines. In addition, EPA is actively engaged in OECD's development and harmonization efforts for guidelines to address environmental fate, endocrine disruptor screening, and efficacy of antimicrobial pesticides.

Tests conducted in accordance with the requirements and recommendations of the applicable OECD protocols can be used to develop data necessary to fulfill the data requirements. However, some of the OECD recommended test standards, such as test

duration and selection of test species, are less restrictive than those recommended by EPA. When using OECD protocols, applicants should be careful to observe the test standards so that the data generated will satisfy the EPA data requirements.

C. Guidelines Specific to Antimicrobials

1. *Comment.* The commenter claimed that guidelines specific to antimicrobials are needed.

2. *EPA's response.* EPA agrees that for certain scientific disciplines or certain studies antimicrobial-specific guidance may be needed. The data required to demonstrate product performance would be very different for an insect repellent or a termiticide versus that needed for sanitizers and disinfectants. Exposure studies could be conducted differently for an antimicrobial used in a food-processing plant versus a conventional pesticide sprayed on an agricultural field. Exposure studies could also be conducted via the same method: A spray can with an insecticide is assessed using the same techniques as a spray can with a disinfectant, with any differences in the assessment being attributed to actual use conditions, such as, indoors versus outdoors or surfaces sprayed. For other scientific disciplines such as toxicology or product chemistry, generally, with a few exceptions, the guidance would be the same. A carcinogenicity, developmental, or reproductive toxicity study would be conducted similarly for an antimicrobial or a conventional pesticide. However, as noted in Unit X.F., the Ames assay may not be useful for assessment of mutagenic potential of antimicrobial pesticides.

XIX. Endangered Species Assessments

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

A. Endangered Species Assessment for Antimicrobials

1. *Comment.* The commenter argued that EPA needs to recognize the manner in

which antimicrobials may result in environmental exposure and the regulations under statutes other than FIFRA in order to promote an effective and efficient approach to regulating antimicrobial pesticides with regard to endangered and threatened species. According to the commenter, antimicrobials are not applied directly to the environment, but environmental exposures from antimicrobial pesticides result from point-source discharges or slow release from pesticide-containing materials.

2. *EPA's response.* EPA agrees that there are differences between antimicrobial pesticides and agricultural pesticides. As discussed in the proposed rule (October 8, 2008, 73 FR 59425), for agricultural pesticides, there is generally greater specificity relative to where a pesticide may be used compared to antimicrobial pesticides. Agricultural pesticides are typically used on crops. As part of its endangered and threatened species assessment, EPA extracts information on county-level crop occurrence and acreage within counties of particular crops from the most recent USDA National Agricultural Statistics Services' Census of Agriculture. Because antimicrobial pesticides are typically not applied directly to the environment, it is easier to delineate and overlay agricultural pesticide use with endangered or threatened species locations than to delineate and overlay antimicrobial pesticides use. Nevertheless, wood preservatives, antifoulant paints and coatings, and other antimicrobial uses, including uses in swimming pool water, industrial slimicides used in recirculating water cooling towers, and paper mills, have the potential for environmental exposures. The Agency is working to refine its endangered species assessment for antimicrobial pesticides to account for the unique mechanisms involved in application and use of antimicrobial pesticides, and the different routes through which antimicrobial pesticides enter the environment.

EPA recognizes that antimicrobials, like any other pesticide product, may be subject to other Federal, State and local laws. FIFRA requires that, before a pesticide may be lawfully sold or distributed in the United States, the product must be registered by EPA,

unless the product is exempt from registration requirements. Prior to registering a pesticide product, EPA must first ensure that the pesticide, when used according to label directions, can be used without posing unreasonable risks to humans and the environment. The registration of a pesticide product, whether it is an antimicrobial or other type of pesticide product, is considered an “action” subject to the Endangered Species Act (ESA). The ESA requires all Federal agencies to ensure that any action they permit or authorize will not result in likely jeopardy to the continued existence of endangered or threatened species, or destroy or adversely modify habitat designated as critical by the U.S. Fish and Wildlife Service (FWS) or National Marine Fisheries Service (NMFS).

In order to ensure EPA’s actions are consistent with the ESA, the Agency must assess the potential for both direct and indirect effects to any potentially exposed threatened or endangered species and critical habitat, independent of whether exposure results from a point-source discharge or the slow release of a pesticide containing material. If effects may occur, EPA consults with the FWS or NMFS to determine whether there may be jeopardy to the species or destruction or adverse modification to habitat designated as critical.

B. Method for Conducting Endangered Species Assessments

1. *Comment.* A commenter claimed that EPA/OPP does not have a mature program currently in place for antimicrobial environmental risk assessment generally. More specifically, the commenter contended that EPA does not have a program in place for assessing potential impacts on endangered and threatened species relevant to antimicrobials and their uses. The commenter argued that until EPA scientifically substantiates data requirements to use in estimating antimicrobial environmental exposures and modeling and the potential for risks from such exposures, it will not be feasible to make any meaningful determinations on potential impacts to endangered species. The commenter concluded that it is thus premature for the EPA to determine how it should

approach antimicrobials with regard to endangered species.

2. *EPA's response.* EPA disagrees with the commenter. EPA has a robust program for completing antimicrobial environmental risk assessments, as outlined in the preamble to the proposed rule (73 FR 59405). Environmental fate studies evaluate the mobility, distribution and dissipation of a pesticide in various compartments of the environment, such as water, soil, air, and sediment. Ecological effects data are used by the Agency to determine the toxicological hazards of pesticides to various nontarget organisms, such as birds, mammals, fish, bees, terrestrial and aquatic invertebrates, and plants. The required environmental fate studies and ecological effects (both plant and animal) data provide the foundation for an environmental risk assessment. EPA's environmental risk assessment for antimicrobials combines environmental fate studies with ecological effects data to determine the potential of the pesticide to cause harmful effects to nontarget organisms and plants. The data requirements that will be codified in the final rule will provide sufficient information for EPA to perform an ecological risk assessment.

EPA/OPP's process for assessing the potential risks of a pesticide to federally-listed threatened or endangered species and their designated critical habitat is described in the document titled "Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency – Endangered and Threatened Species Effects Determinations" (Ref. 13). Appendix A to that document – "Overview of OPP's Screening-Level Ecological Risk Assessment Process for Antimicrobial Pesticides" – explains both the data needed and the process that would be used by EPA to assess potential risks to endangered and threatened species from antimicrobial pesticides.

EPA's assessment of potential impacts on endangered and threatened species begins with a screening level assessment to determine if there is a potential concern. When the screening-level ecological risk assessment raises potential concerns related to a listed species, EPA then conducts a species-specific evaluation to refine the assessment. The

more refined assessment should involve clear delineation of the action area associated with the proposed use of the pesticide and best available information on the temporal and spatial co-location of the listed species with respect to the action area. EPA notes that with the publication of the proposed rule, the discussion in Appendix A is out of date. In response to comments received on the proposed antimicrobial data requirements, EPA indicated it is no longer relying on its proposed approach classifying use patterns as high/low or minimal/significant exposure uses with regard to ecological effects testing. However, the Agency's basic approach to endangered species risk assessments, which combine environmental fate studies with ecological effects data to determine the potential of the pesticide to cause harmful effects to endangered species, has not changed. In addition, the Agency will conduct an assessment for antimicrobial pesticides with down-the-drain uses, as described in response to comment 134.1 in the Response to Comments Document in the docket. The codified data requirements and the down-the-drain assessment will extend EPA's Antimicrobial Division's ability to understand the potential impacts of antimicrobial pesticides on endangered species.

EPA cannot wait to comply with the ESA until newer, more advanced, models are available or additional data needs are determined. Federal agencies must comply with the ESA by performing their assessments and analyses using the best scientific and commercial data available. As a part of Registration Review, EPA is conducting species-specific environmental risk assessments that will allow EPA to determine whether the antimicrobial pesticide product has "no effect" or "may affect" federally-listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide product's use "may effect" a listed species or its designated critical habitat, the Agency will consult with the FWS and/or NMFS, as appropriate.

XX. Endocrine Disruption

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

1. *Comment.* The commenters noted that EPA did not include any studies to assess endocrine disruption effects.

2. *EPA's response.* The commenter is correct that EPA did not include, within proposed part 158, subpart W, studies whose sole purpose is to assess endocrine disruption effects in avian and aquatic species. The Agency is also not including such studies in this final rule.

With regards to toxicology data requirements, as required by FIFRA and FFDCA, EPA reviews a toxicological data base of numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. EPA reviews these data and selects the most sensitive endpoints for relevant risk assessment scenarios from the existing toxicological data base.

With regards to ecotoxicity data requirements, as required by FIFRA and FFDCA, EPA reviews a nontarget organism data base of numerous studies to assess potential adverse outcomes from exposure to chemicals. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. EPA reviews these data and selects the most sensitive endpoints for relevant risk assessment scenarios from the existing nontarget organism database.

Through a separate effort, the Agency has also developed a screening battery to identify chemicals that may have effects on the hormone systems of humans and wildlife. As required under FFDCA section 408(p), the Agency developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a “naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier I consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier I screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA issued test orders/data call-ins for 58 pesticide active ingredients and 9 inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Under FFDCA section 408(p) the Agency must screen all pesticide chemicals, including antimicrobials. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the EDSP including the status and test guidelines, please visit the website: <http://www.epa.gov/endo/>.

XXI. Effective Date of Final Antimicrobial Data Requirements

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments Document available in the docket to this rule.

1. *Comment.* Several commenters have expressed concern over when the final rule would take effect. One commenter stated that compliance with the Administrative Procedures Act requires EPA to apply any final rulemaking on data requirements for antimicrobials only to applications submitted after the effective date; otherwise, EPA would be promulgating the final rule retroactively. The commenter also asserted that EPA should be consistent in its implementation of effective dates, noting that EPA did not impose new data requirements on pending conventional pesticide registrants when the conventional pesticide rules were revised. A second commenter suggested that registrations pending at the time of the final rule publication be given conditional registration under section 3(c)(7) of FIFRA or under section 3(c)(5) if the requirements of part 161 have been met, and that implementation of the part 158, subpart W data requirements occur at the time of periodic registration review. Another commenter noted that EPA has provided reasonable notice to registrants and recommends that EPA implement the rule as soon as technically feasible. A different commenter questioned whether additional Pesticide Registration Improvement Act (PRIA) registration fees would be required for pending applications if the registrant did not meet new data requirements and withdrew the application, or if the Agency issued a determination that it cannot grant the application.

2. *EPA's response.* EPA will follow an approach similar to that used for conventional pesticides following the promulgation of that portion of 40 CFR part 158.

As previously discussed, the final rule for antimicrobials contains 11 "new" data requirements. "New" means that the data requirement has never been required, or has rarely been required on a case-by-case basis and has not been routinely considered during

the Agency's evaluation of the data needed for the purpose of risk assessment. The new data requirements being codified include eight that were proposed and three that have been added based on public comments received about the proposed rule.

EPA recognizes that during early implementation of 40 CFR part 158, subpart W not all application packages may have all of the newly-required data. Therefore during early implementation of 40 CFR part 158, subpart W, EPA will accept for review and evaluation application packages that may not have all of the newly required data in appropriate cases supported by adequate justification. This early implementation period could extend up to 2 years post-promulgation for situations in which a more time-intensive new study is missing but could be less for other situations, such as for less time-intensive new studies. The applicant should address the issue of timing (i.e., why the data are not yet submitted and when the data can be submitted) with respect to any missing newly-required data, in their justification.

EPA is statutorily required to evaluate the proposed pesticide thoroughly to ensure that it will not unreasonably harm human health or the environment. For pesticides needing FFDCA section 408 tolerances, EPA is statutorily required to make a safety finding that the pesticide can be used with "reasonable certainty of no harm." In cases where the application may not have all the required data, EPA would evaluate whether a registration determination or a safety finding can be made based on the available data or on the results of other studies in the pesticide's data base. If there is insufficient information, and if the data base does not provide information on the endpoints that would be tested, or data provided by the applicant or information in the data base shows evidence of effects, EPA may not be able to make a registration decision or safety finding. In such cases, the application may be denied or the applicant may choose to withdraw the application pending completion of the needed data. In some cases, conditional registrations may be appropriate for consideration. Among other things, a determination that the proposed use

will not significantly increase the risk of unreasonable adverse effects on the environment will need to be made. If EPA can make that determination and the other elements for a conditional registration are met, then a conditional registration may be appropriate and the new data required as a condition of registration. If there is a basis for granting a conditional registration, then the timeframe for conditioning the registration would be determined based on factors such as the required studies involved and the length of time required to conduct those studies.

Importantly, it should be noted that acceptance of an application for processing during early implementation of 40 CFR part 158, subpart W, that does not result in a conditional registration, does not permanently relieve the applicant from providing the newly required data. Based on the particular case involved, the Agency will employ appropriate mechanisms, for example, through a data call-in or through the registration review process, to ensure the generation and submission of any missing newly-required data.

With respect to pending applications that are withdrawn, additional Pesticide Registration Improvement Act (PRIA) registration fees will generally only be required if the applicant seeks to pursue the action again by submitting a new application (and addressing the deficiencies in the original application). In withdrawal situations, the Agency provides a refund for any work that the Agency did not perform on the application following a withdrawal. Similarly, a determination that the application cannot be granted does not require additional PRIA registration fees. In that case, additional fees will only be incurred if the application is subsequently withdrawn or denied, and the applicant seeks to pursue the action again and submits a new application.

XXII. Economic Analysis

This unit summarizes the significant public comments and EPA's response to those comments. A more detailed discussion can be found in the Response to Comments

Document available in the docket to this rule.

A. Comparing Estimates of Cost of the Proposed Rule

1. *Comment.* A commenter performed an independent economic analysis (EA) for the proposed rule. According to the commenter's analysis, the cost of proposed part 158, subpart W is greater than that estimated by the EPA. In addition, the unit test costs and frequency of tests used in the commenter's analysis are different than EPA's.

2. *EPA's response.* EPA reviewed the commenter's analysis and based on that review revised the EA for the final rule. EPA's evaluation of the commenter's EA indicated there were the following differences between the two EAs:

- The cost estimates used for the studies,
- Overhead costs were included by the commenter, but not by EPA,
- Costs for Registration Review (see Unit XXII.C.).

The differences between the cost of the proposed rule as estimated by the commenter and the cost as assessed by the Agency for new registrations are explained in the following subunits.

i. *How data requirement costs are calculated.* The annual cost of a data requirement is the product of three factors: Unit test cost, probability of the test being required, and the number of registrations in the industry per year for the registration type and use. That is: "Industry cost of a data requirement = Unit test cost x test probability x number of registrations." These costs are summed for all data requirements, uses, and registration types to get the total annual cost of the data requirements for the industry.

ii. *Differences in unit test costs.* EPA acknowledges that there are significant differences between the Agency's analysis and the commenter's analysis regarding the unit test costs. According to the commenter's EA, the costs were provided to them by their client's technical consultants, and are "based on quotes from laboratories, actual experience, and professional judgment." The commenter did not provide sufficient

information with which to evaluate the commenter's test cost estimates. Additionally, EPA notes that having all test cost estimates ending in zero could be indicative of estimation.

EPA's unit test costs for each data requirement were obtained by contacting established contract research organizations (CROs) to assess what the labs would charge to conduct studies according to specific designs provided by EPA, or as specified in OPPTS guidelines (now OCSPP guidelines). Upper and lower cost estimates were requested. For each test, the upper cost estimates from each CRO were averaged to obtain a high average estimate. A similar calculation was done for the lower cost estimate. EPA's estimate is the average of the high and low average estimates.

iii. *Test costs and overhead costs.* The commenter added 30 percent to their test cost estimates to account for the overhead of the registrants managing and overseeing the tests they contract to the labs. EPA acknowledges that there are costs other than test costs associated with registering and maintaining the registrations of pesticide products. Overhead is not a new cost, attributable to the rule, and EPA does not believe that overhead costs will change significantly as a result of codifying data requirements for antimicrobials. EPA does not include overhead costs in its economic analyses of data requirements rules because the Agency accounts for other registration costs such as overhead in the Information Collection Request (ICR) for FIFRA Section 3 Registration under the Paperwork Reduction Act.

iv. *Test probabilities.* EPA's test probabilities (the probabilities of tests being required for a registration action) were based on a sample of 70 actual antimicrobial registration actions out of 90 relevant new registration actions during the 6 year period beginning 2000 and ending 2005, supplemented with EPA's scientific judgment. The time period (2000-2005) was chosen for EPA's EA because the analysis in the EA was started in 2006. The commenter claims to have based the test probabilities used to make their

estimates on a sample of 29 registration review cases (not new registrations) occurring between 2008 and 2010.

v. *Factors which drive costs for new registrations.* To determine the influence of the previously-discussed factors on the difference between the commenter's and EPA's estimates, EPA performed the following analysis on the data requirements costs and incremental costs using the same unit test costs and test probabilities used in the proposed rule:

- To account for the effect of the unit test costs on the data requirements costs and incremental costs, EPA substituted the commenter's unit test costs without overhead into EPA's analysis of the proposed rule using EPA's test probabilities and number of registrations. If there were no changes, this would indicate that the test costs were not driving the differences in estimates.

- To account for the effect of test probabilities and number of registrations, EPA substituted the commenter's unit test costs with overhead into EPA's analysis. In this case, the difference between the EPA's and the commenter's analysis is contained in the test probabilities and number of registrations. If there were no changes, this would indicate that the test probabilities and number of registrations were not driving the differences between the two analyses. Since the commenter includes overhead in their analysis, overhead was included in this comparison to make other things equal so that the differences in test probabilities and number of registrations could be isolated.

vi. *Results.* The results of the factor analysis are presented in the following Table 1.

Table 1.—Comparison of Data Requirement Costs and Factors for New Registrations

Factors	A	B	C	D
Unit Test Costs according to:	EPA Proposed Rule	Commenter without overhead	Commenter with 30 percent overhead	Commenter with 30 percent overhead
Test Probabilities according to:	EPA	EPA	EPA	Commenter
Number of Registrations according to:	EPA	EPA	EPA	Commenter
Data Requirement Cost according to Proposed Rule (\$ millions)	\$15.0	\$19.9	\$25.5	\$25.9
Cost of Proposed Rule (Incremental Costs) (\$ millions)	\$3.9	\$7.6	\$9.8	\$9.2

Column A exhibits the data requirements and incremental costs from EPA's EA of the proposed rule. In column B, the data requirements and incremental costs are calculated using the commenter's unit test costs without overhead costs, but EPA's test probabilities and number of registrations. Column C is the same as column B, but with overhead costs included. Finally, column D exhibits the data requirements and incremental costs with overhead as calculated by the commenter.

The result of the first factor analysis is demonstrated by comparing column A to column B. In this case, the difference between the two columns is the unit test costs. Inserting the commenter's unit test costs, without overhead, into the cost estimates with EPA's test probabilities and number of registrations leads to over a 30 percent increase in data requirements cost and a nearly 100 percent increase in incremental costs.

The result of the second factor analysis is demonstrated by comparing columns C and D. In this case, the difference between the two columns is in the test probabilities and number of registrations. While individual test probabilities may be different in EPA's and the commenter's analyses, the overall effect of the products of test probabilities and number of registrations, when summed with the unit test costs, including overhead, are

similar in both of these analyses. The resulting differences in data requirements cost and incremental costs are less than 2 percent and about 6 percent, respectively. Therefore, EPA concludes that any differences in test probabilities and number of registrations used as input parameters in the calculations do not have a significant effect on the total data requirement cost of new registrations.

Comparisons across columns A, B, and C also provide information on the portion of the cost difference accounted for by overhead costs. Columns A, B, and C compare the cost of data requirements using the unit test cost estimates of EPA and those of the commenter with and without overhead. The overhead costs account for more than one-half of the difference in the total cost of the data requirements, but less than 40 percent of the difference in incremental costs (the incremental cost is the increase in costs between the baseline (the existing data requirements in part 161) and proposed part 158, subpart W).

From this comparison, EPA makes the following conclusions. First, differences in test probabilities and number of registrations do not have a significant impact on the cost of the rule. Second, even if EPA and the commenter used the same probabilities and test costs, inclusion of overhead costs by the commenter would result in a 30 percent difference in costs. Finally, when the overhead costs are removed from the commenter's analysis, differences in unit test costs between EPA and the commenter account for most of the differences in the estimates of the cost of the rule for new registrations.

vii. *Revised test costs.* In light of the results of the comparison between EPA's and the commenter's EA, EPA sought to verify its unit test cost estimates. To examine the costs submitted by ACC, EPA resurveyed the cost of conducting studies for 30 data requirements: The criteria for selecting which test's cost to update included how the difference in estimates would impact on the cost of the rule, the magnitude of the differences in estimates, and the age and source of EPA's estimates. EPA's data gathering methodology is reproducible, and based on actual data. EPA does not adjust the lab's cost

estimates, i.e., the costs are used as obtained from the laboratory. Under the Information Quality Act (IQA), EPA must ensure and maximize the quality, objectivity, utility, and integrity of the data used in its analyses.

The resurveyed test costs are used in the EA for the final rule. EPA is using its cost estimates because it has revised its most relevant and oldest unit test cost estimates. In addition, the commenter did not provide a basis or sufficient explanation that would meet the standards of the IQA to justify EPA's accepting the commenter's costs. For additional information see response to comment 40.1 in the Response to Comments Document and the final economic analysis, both in the docket.

B. Impact on Small Businesses

1. *Comment.* A commenter claimed that EPA underestimated costs, is not fully complying with the Regulatory Flexibility Act (RFA) and the Small Business Regulatory Enforcement Fairness Act (SBREFA), and must prepare an Initial Regulatory Flexibility Assessment (IRFA). In addition, the commenter argued that small businesses will be adversely affected, that there will be an "increased disparity between registrants and a more uneven playing field," and finally, that a SBREFA analysis should have been conducted.

2. *EPA's response.* EPA acknowledges that the cost of the data requirements would likely be a larger percentage of a small business's revenues, but did not find that the rule would have a significant adverse economic impact on a substantial number of small firms.

A regulatory flexibility analysis examines the type and number of small entities potentially subject to the rule, recordkeeping and compliance requirements, and significant regulatory alternatives, among other things. RFA, as amended by SBREFA, requires EPA to consider the economic impact of proposed rules on small entities. RFA requires EPA to prepare an IRFA for each proposed rule, when the rule will have a significant economic

impact on a substantial number of small entities.

To comply with RFA, EPA did a retrospective analysis of what the additional costs would have been on actual new registrations if the proposed rule had been in effect during 2000-2005. This analysis did not indicate a significant impact on a substantial number of small entities; instead, the analysis indicated that 5 percent of small firms (25 out of 500) are likely to experience some impact and only 2.8 percent of small firms (14 out of 500) are likely to experience an economic impact of 3 percent or more of gross sales. Based on this analysis, EPA certified that the proposed rule would not have a significant adverse economic impact on a substantial number of small firms. As a result, EPA did not have to conduct an IRFA nor convene a SBREFA Panel for the proposed part 158, subpart W rule.

In the EA for the final rule, EPA reestimated the SBREFA analysis with revised unit test costs and changes in data requirements.

- About 23 small firms (almost 5 percent) are likely to experience an economic impact of 3 percent or more of gross sales, and
- About 26 small firms, (over 5 percent) are likely to experience an economic impact of 1 percent or more of gross sales.

Hence, had these results been estimated at the proposal stage, EPA would still have concluded that there would not be a significant impact on a substantial number of small entities.

C. Cost of New Data Requirements on Registration Review

1. *Comment.* A commenter stated that EPA has not accurately stated the potential costs and benefits, as required by Executive Order (EO) 12866. In particular, EPA has not included the impact of incremental costs of new data requirements on registration review, or the cost of consultations. The commenter also claims that under the Paperwork Reduction Act (PRA), EPA should include the paperwork burden costs of registration review for existing registrants.

2. *EPA's response.* EO 12866 requires the Agency to submit to OMB for review significant regulatory actions. EPA complied with EO 12866 during 2008 by submitting drafts of both the economic analysis and the proposed rule to OMB. The changes that were made to the proposed rule as the result of OMB's review were included in the docket for the proposed rule. The Agency notes that one purpose of soliciting comments on the economic analysis at the proposal stage is to get input on where the Agency might improve the economic analysis.

The commenter is not correct in asserting that EPA did not include the impact of incremental costs. The Agency has captured the anticipated costs necessary for complying with the regulations. See the final Economic Analysis (Ref. 1) in the docket for a more detailed discussion, particularly sections 5.3 and 5.5.

The commenter is correct in that the costs of fulfilling the 11 "new" data requirements during registration review were not considered in the Agency's economic analysis of the proposed part 158, subpart W data requirements. EPA agrees with the commenter that registrants of existing antimicrobial products will incur costs during registration review. In fact, EPA relied on the 2005 EA conducted for the Registration Review Rule. When registration review was proposed, EPA prepared an economic analysis of that program, which estimated the cost of data requirements and paperwork burden according to what would likely be required in registration review for existing registrants. The 2005 registration review EA estimate of data requirement costs for existing antimicrobial pesticides was based on what would likely be required for a sample of antimicrobial active ingredients. This would have included all tests that would have been required at that time, i.e., those in current practice whether or not in part 158.

However, proposed part 158, subpart W included "new" tests, which were not anticipated when the economic analysis of the registration review process was completed. In a final economic analysis for part 158, subpart W, EPA addresses the additional

registration review costs for these 11 “new” studies, as well as other changes from the proposed rule to the final rule, including changes made as a result of the comments received. The incremental impact for Registration Review is \$ 6.8 million.

The commenter is also correct that EPA did not include the cost of consultation in its economic analysis. Consultations are longstanding, commonly used, and valuable processes in EPA’s Pesticide Program and are beneficial to both EPA and the applicants. However, consultations are not mandatory, and based on comments received EPA has removed all references to consultations from the final data requirements tables. See Unit V.C. for additional information on the use and purpose of consultations.

XXIII. References

As indicated under **ADDRESSES**, a docket has been established for this rulemaking under docket ID number EPA-HQ-OPP–2008–0110. The following is a listing of the documents that are specifically referenced in this proposed rule. The docket includes these documents and other information considered by EPA in developing this rule, including documents that are referenced within the documents that are included in the docket, even if the referenced document is not physically located in the docket. For assistance in locating documents, please consult the technical contact listed under **FOR FURTHER INFORMATION CONTACT**.

1. USEPA, Final Economic Analysis of Changes in Data Requirements for Antimicrobial Pesticides, (March 13, 2013).
2. USEPA, “Data Requirements for Pesticide Registration; Final Rule” (49 FR 42856, October 26, 2007)(FRL-8106-5).
3. ACC Biocides Panel; “Regulation of Antimicrobials that are Indirect or Secondary Direct Food Additives;” (February 2, 2006).
4. CMA Biocides Panel; “Comments on EPA’s September 17, 1999 Proposed Rule on Registration Requirements for Antimicrobial Pesticide Products and Other Pesticide

Regulatory Changes for Codification; (January 18, 2000).

5. ACC Biocides Panel; Memorandum to Frank Sanders, “EPA’s Current Interpretation of the Antimicrobial Reform Technical Corrections Act and Section 2(bb) of FIFRA is Inconsistent with the Statutes;” (November 3, 2000).

6. ACC Biocides Panel; “EPA/FDA Jurisdiction for Food Contact Antimicrobials;” (July 17, 2003).

7. Grizzle, Charles L.; representative of Albright & Wilson Americas, Inc., letter to Lynn R. Goldman; (September 11, 1997).

8. ChemReg International, L.L.C.; Tiered Testing for Risk Assessment of Antimicrobial Pesticides; (September 12, 2002).

9. Goldberg, Seth; “Section 2(bb) of FIFRA; Dual Jurisdiction Over Food Contact Antimicrobials; (April 27, 2001).

10. ACC Biocides Panel; “Comments on The Preliminary Risk Assessment for 1,4-Bis(bromoacetoxy)-2-butene (BBAB);” (August 6, 2001).

11. ACC Biocides; Hasmukh C. Shah letter to Frank T. Sanders; (August 3, 2000).

12. Edwards, Deborah; OPP Response to CropLife letter of May 29, 2009; (June 26, 2009).

13. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency – Endangered and Threatened Species Effects Determinations (January 2004) (*see www.epa.gov/espp/consultation/ecorisk-overview.pdf*).

14. Portier; SAP Waiver; (April 4, 2011).

XXIV. FIFRA Review Requirements

In accordance with FIFRA section 25(a), a draft of this final rule was submitted to the FIFRA SAP. EPA requested the FIFRA SAP to waive its review of the final rule based

on the fact that the SAP, in 2008, had waived review of the proposed rule. The final rule does not contain any new scientific issues warranting additional review by the SAP. The SAP waived its review on April 4, 2011, stating that “[t]he final rule does not contain scientific issues that the Panel has not previously considered” (Ref. 14).

In accordance with FIFRA section 25(a), EPA has submitted a draft of the final rule to the appropriate Congressional Committees and the Secretary of the Department of Agriculture. There were no comments in response to these submissions.

In accordance with FIFRA section 21(b), EPA submitted a draft of the final rule to the Secretary of Health and Human Services (HHS), and their comments were reviewed and addressed in this final rule.

XXV. Statutory and Executive Order Reviews

A. Executive Order 12866: Regulatory Planning and Review and Executive Order 13563: Improving Regulation and Regulatory Review

Under Executive Order 12866 (58 FR 51735, October 4, 1993), this action is a “significant regulatory action” because the Office of Management and Budget (OMB) determined that this action might raise novel legal or policy issues arising out of legal mandates, the President’s priorities, or the principles set forth in the Executive Order.

Accordingly, EPA submitted this action to OMB for review under Executive Orders 12866 and 13563 (76 FR 3821, January 21, 2011). Any changes made in response to OMB recommendations have been documented in the docket for this action as required by Executive Order 12866.

EPA has prepared an EA of the potential costs associated with this action, entitled “Final Economic Analysis of Changes in Data Requirements for Antimicrobial Pesticides” (Ref. 1), a copy of which is in the docket. This final EA evaluates the potential benefits

and costs expected as a result of registrations and registration reviews. The EA is briefly summarized here.

In its analysis, the Agency considered the potential, additional costs for the registration of new antimicrobial pesticides or new uses of currently registered antimicrobial pesticides, as well as the potential, additional costs incurred during the registration review of existing antimicrobial pesticides.

Based on comments received during the public comment period, the following changes were made to the rulemaking, and are therefore reflected in the final EA:

- One proposed data requirement will not be codified: Non-dietary ingestion exposure. The test cost is \$75,000. In the proposed rule, EPA expected to receive the test 0.8 times per year, representing an annual industry savings of \$63,125.
- EPA revised certain of the data requirements from “NR” or “CR” to “R,” or vice-versa.

Based on comments received, three new data requirements were added: Simulation test to assess the biodegradability of chemicals discharged in wastewater, simulation test – aerobic sewage treatment: Activated sludge units, and nature of the residue on surfaces. The rationale for these three new studies is described in Unit III.B.

The estimated costs for both registration review and for a registration action for the three newly-required data requirements are:

1. *Simulation tests to assess the biodegradability of chemicals in discharged wastewater and simulation test – aerobic sewage treatment: activated sludge units.* Both of these studies are used as part of the down-the-drain analysis for antimicrobials. The studies are conditionally required for all use patterns, except for the aquatic areas use pattern, for which the study is not required. EPA does not have an estimate for the cost of either of these studies; instead, for the EA, EPA used the value \$33,000, which is the cost of the porous pot test. The Agency expects, however, that the cost of the simulation tests

will be less than this amount. For registration review, EPA expects to receive the porous pot test or one of the simulation tests up to 8.5 times per year, for an annual industry cost of \$280,500. For new registrations, EPA expects to receive either of the studies up to 7.5 times per year, for an annual industry cost of \$247,500. The total annual cost is \$528,000.

2. *Nature of residue on surfaces.* This test is part of the residue chemistry data requirements, and is conditionally required for all use pattern categories. The test cost is \$95,000. For registration review, EPA expects to receive this test 1.3 times per year, for an annual industry cost of \$118,750. For new registrations, EPA expects to receive this test up to 0.5 times per year, for an annual industry cost of \$44,333. The total annual cost is \$163,083.

Many test notes for data requirements were revised based on comments received. Data requirements for certain use patterns were changed from “NR” or “CR” to “R,” while others were changed from “R” to “CR.” Because the cost of the rule depends, in part, on the probabilities of the tests being required, these revisions have resulted in a modification of the cost of the rule. Instead of estimating the cost of each change individually, the Agency reestimated the potential cost of the regulation as a whole, taking into account the changes discussed previously.

Based on comments received, EPA has updated the unit test costs for 30 selected tests. The criteria for selecting which test’s cost to update included:

- How changing the cost estimates would impact on the cost of the rule,
- The magnitude of the difference between EPA’s cost estimate and the commenters’ cost estimate, and
- The length of time since EPA’s cost estimate was last updated.

EPA estimated the annual cost of registering a new antimicrobial pesticide or new use of currently-registered antimicrobial pesticides, taking into account both the changes in data requirements and in unit test costs. Both the total annual industry costs and the

newly-imposed costs were estimated. The updated test costs plus exposure and other test costs revisions since the proposed rule increased the cost of the rule by about 23 percent compared to the proposed rule. The estimated total annual industry costs of the final rule is expected to be about \$19.3 million, which is approximately 29 percent higher than the cost of the proposed rule. The difference between the baseline costs (the existing data requirements that were codified in 1984) and the cost of the Agency's current practices is about \$1 million annually. The difference between the baseline costs and the final rule costs, i.e., the incremental costs, is approximately \$8.2 million annually. Under the final rule, the average cost per registration action of a new antimicrobial active ingredient is approximately \$1 million to \$5 million.

For existing chemicals, data requirements in part 158, subpart W are relevant to the registration review program which began to replace the reregistration program in 2006 as a means of systematically reevaluating existing registrations against the standards of FIFRA.

EPA has evaluated the impact of the data requirements being codified in this final rule on registrants of existing chemicals undergoing registration review whose active ingredient data bases do not contain all of the new data requirements. The average additional cost of registration review as a result of the new data requirements is estimated to be about \$588,000 for wood preservatives, \$284,000 for food and indirect food uses, and \$260,000 for all other uses. For registration review, the total annual cost is \$6.8 million.

As required, EPA conducted an analysis of the impact of this final rule on small businesses, as discussed in the Unit XXV.C.

B. Paperwork Reduction Act (PRA)

The information collection requirements contained in this rule have been submitted for approval to OMB under the PRA, 44 U.S.C. 3501 *et seq.* At the time of the proposed rule, EPA prepared a supporting statement for amending an ICR, entitled "Data

Requirements for Antimicrobial Pesticides (Proposed Rule)” and identified by EPA ICR No. 2318.01, a copy of which is in the docket.

Under PRA, “burden” means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency.

The information collection activities related to the submission of data to EPA in order to register, amend or retain a new or existing pesticide product or obtain a tolerance for that product are already approved by OMB under PRA. As such, the supporting statement only addresses the proposed changes to the data requirements that impact the information collection activities related to antimicrobial pesticides. The procedures for submitting data to EPA under FIFRA and FFDCA are not changed in this proposal, and are already approved by OMB in the following ICRs:

1. *Tolerance ICR*. Data Submission Activities Associated with Tolerance Actions (currently approved under OMB Control No. 2070-0024 (EPA ICR No. 0597));

2. *Registration ICR*. Data Submission Activities Associated with the Application for a New or Amended Registration of a Pesticide (currently approved under OMB Control No. 2070-0060 (EPA ICR No. 0277)); and

3. *Reregistration, Special and Registration Review ICR*. Data Submission Activities Associated with the Generation of Data for Special Review or Registration Review (currently approved under OMB Control No. 2070-0174 (EPA ICR No. 2288)).

These three program activities are an integral part of the Agency’s pesticide program, including antimicrobial pesticides, and the corresponding ICRs are regularly renewed every 3 years as required by PRA. The total estimated average annual public reporting burden currently approved by OMB for these various activities range from 8 hours to approximately 3,000 hours per respondent, depending on the activity and other factors surrounding the particular pesticide product.

In the supporting statement the Agency estimates that the typical, current annual paperwork burden for registrants per antimicrobial pesticide registration is 194 burden hours and \$12,631. The total annual registrant paperwork burden and costs for data submission activities for antimicrobial pesticides applicants and registrants will be updated accordingly in the ICRs specified in this discussion during the next, appropriate ICR renewal cycle.

An agency may not conduct or sponsor, and a person is not required to respond to an information collection request unless it displays a currently valid OMB control number, or is otherwise required to submit the specific information by a statute. The OMB control numbers for EPA's regulations codified in Title 40 of the Code of Federal Regulations, after appearing in the preamble of the final rule, are further displayed either by publication in the **Federal Register** or by other appropriate means, such as on the related collection instrument or form, if applicable. The display of OMB control numbers for certain EPA regulations is consolidated in a list at 40 CFR 9.1.

C. Regulatory Flexibility Act (RFA)

The RFA, 5 U.S.C. 601 *et seq.*, generally requires an Agency to prepare a regulatory flexibility analysis of any rule subject to notice and comment rulemaking requirements under the Administrative Procedure Act, 5 U.S.C. 551-553, or any other statute unless the agency certifies that the rule will not have a significant economic impact on a substantial number of small entities. Small entities include small businesses, small organizations and small governmental jurisdictions.

For purposes of assessing the impacts of this final rule on small entities, small entity is defined as:

1. A small business as defined by the Small Business Administration's (SBA) regulations at 13 CFR 121.201, which is based on either the maximum number of employees or on the sales for small businesses in each industry sector, as defined by a 6-

digit NAICS code, and for this rule is a producer of pesticide products (NAICS 32532), antifoulants (NAICS 32551), antimicrobial pesticides (NAICS 32561) or wood preservatives (NAICS 32519), importers of such products, or any person or company who seeks to register an antimicrobial, antifoulant coating, ballast water treatment, or wood preservative pesticide or to obtain a tolerance for such a pesticide;

2. A small governmental jurisdiction that is a government of a city, county, town, school district or special district with a population of less than 50,000; or

3. A small organization that is any not-for-profit enterprise which is independently owned and operated and is not dominant in its field.

After considering the economic impacts of this final rule on small entities, I certify that this action will not have a significant economic impact on a substantial number of small entities. The factual basis for the Agency's determination is presented in the small entity impact analysis prepared as part of the Economic Analysis for this final rule (Ref. 1), and is summarized in this unit.

EPA has determined that this rulemaking does not impact any small governmental jurisdictions or any small not-for-profit enterprise because these entities are rarely pesticide applicants or registrants. As such, EPA has assessed the impacts on small businesses. Some of the small entities directly regulated by this rulemaking are in the pesticide and other agricultural chemical manufacturing industry sector (NAICS code 325320). Firms in this sector are considered small under the SBA definition if they employ 500 or fewer people. The economic analysis for the final rule specifies the NAICS code used for each of the firms analyzed.

EPA estimates that 750 unique parent companies constitute the total universe of pesticide antimicrobial registrants. Of these, based on the SBA definition of a small business and the available sales data for these firms, EPA estimates that 500, or approximately 67 percent, qualify as a small business. When considering both registration

review and new registrations, on average each year about 30 small businesses would have incurred additional costs under this rule. EPA estimates that:

- About 23 small firms (almost 5 percent of the 500 small antimicrobial firms) subject to this regulation are likely to experience an economic impact of 3 percent or more of gross sales,
- About 3 small firms (0.6 percent of the 500 small antimicrobial firms) subject to this regulation are likely to experience an economic impact of greater than 1 percent but less than 3 percent of sales revenues, and
- About 3 small firms (0.6 percent of the 500 small antimicrobial firms) subject to this regulation are likely to experience an economic impact of greater than 0 percent, but less than 1 percent of sales revenues.

In addition, there are also opportunities for small entities to lower their potential costs. The proposed data requirements in many instances are tiered, with higher-tiered testing triggered on the results of lower-tiered testing. EPA encourages registrants to consult with the Agency to ensure that only the required data is submitted. If available, open literature or the same tests on similar products, or alternative means to meet data requirements, such as QSAR, can be submitted for Agency consideration. Some firms may have surrogate data or they may share the cost of generating data. These may present opportunities for cost savings by small entities, and all other applicants as well, while allowing the Agency to fulfill its role of making pesticide regulatory decisions that protect the general population, sensitive sub-populations, and the environment.

D. Unfunded Mandates Reform Act (UMRA)

Title II of UMRA, 2 U.S.C. 1531-1538, establishes requirements for Federal agencies to assess the effects of their regulatory actions on State, local, and tribal governments and the private sector. EPA has determined that this final rule does not contain a Federal mandate that may result in expenditures of \$100 million or more for

State, local, and tribal governments, in the aggregate, or the private sector in any one year.

As described in Unit XXV.A., the incremental costs for this final rule is estimated at approximately \$8.3 million (for registration actions) and \$6.8 million (for registration review) per year for the private sector, which is below the \$100 million threshold. Since State, local, and tribal governments are rarely pesticide applicants, this rule is not expected to significantly or uniquely affect small governments, nor does this rule contain any regulatory requirements that might significantly or uniquely affect small governments. Accordingly, this rule is not subject to the requirements of sections 202 and 205 of UMRA.

This rule is also not subject to the requirements of section 203 of UMRA because it contains no regulatory requirements that might significantly or uniquely affect small governments. As stated previously, State, local, and tribal governments are rarely pesticide applicants.

E. Executive Order 13132: Federalism

This action does not have federalism implications, because it will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132 (64 FR 43255, August 10, 1999). Since States or local governments are rarely pesticide applicants or registrants, this final rule would seldom affect a State or local government. Thus, Executive Order 13132 does not apply to this rule.

In the spirit of Executive Order 13132 and consistent with EPA policy to promote communication between EPA, and State and local governments, EPA specifically solicited comment on the proposed rule from State and local officials. EPA did receive comments on substantive parts from local sanitation districts and associations representing their interests. Their comments are addressed in the Response to Comments Document in the

docket, and, as appropriate, revisions were made for the final rule.

F. Executive Order 13175: Consultation and Coordination with Indian Tribal Government Implications

This action does not have tribal implications, as specified in Executive Order 13175 (65 FR 67249, November 9, 2000). At present, no tribal government holds, or has applied for, a pesticide registration. Thus, Executive Order 13175 does not apply to this action. In the spirit of the Order, and consistent with EPA policy to promote communications between the Agency and Indian tribes, EPA specifically solicited comment on the proposed rule from tribal officials. No comments were received.

G. Executive Order 13045: Protection of Children from Environmental Health and Safety Risks

EPA interprets Executive Order 13045 (62 FR 19885, April 23, 1997), as applying only to those regulatory actions that concern health or safety risks, such that the analysis required under section 5-501 of the Executive Order has the potential to influence the regulation. This final rule is not subject to Executive Order 13045 because it is not economically significant as defined by Executive Order 12866, and because the Agency does not have reason to believe the environmental health or safety risks addressed by this action present a disproportionate risk to children. This rule does not propose an environmental standard that is intended to have a negatively disproportionate effect on children. To the contrary, this rule is intended to provide added protection to children from antimicrobial pesticide risk. EPA will use the data and information obtained by this action to carry out its mandate under FFDCA to give special attention to the risks of pesticides to sensitive groups in early lifestages, especially infants and children.

H. Executive Order 13211: Actions Concerning Regulations that Significantly Affect

Energy Supply, Distribution, or Use

This final rule is not subject to Executive Order 13211 (66 FR 28355, May 22, 2001) because it is not likely to have any adverse effect on the supply, distribution, or use of energy.

I. National Technology Transfer and Advancement Act (NTTAA)

Section 12(d) of NTTAA, 15 U.S.C. 272 note, directs EPA to use voluntary consensus standards in its regulatory activities unless to do so would be inconsistent with applicable law or otherwise impractical. Voluntary consensus standards are technical standards (e.g., materials specifications, test methods, sampling procedures, and business practices) that are developed or adopted by voluntary consensus standards bodies. NTTAA directs EPA to provide Congress, through OMB, explanations when the Agency decides not to use available and applicable voluntary consensus standards. This action does not involve technical standards. Therefore, EPA did not consider the use of any voluntary consensus standards.

J. Executive Order 12898: Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations

Executive Order 12898 (59 FR 7629, February 16, 1994) establishes Federal executive policy on environmental justice. Its main provision directs Federal agencies, to the greatest extent practicable and permitted by law, to make environmental justice part of their mission by identifying and addressing, as appropriate, disproportionately high and adverse human health or environmental effects of their programs, policies, and activities on minority populations and low-income populations in the United States.

EPA has determined that this final rule will not have disproportionately high and

adverse human health or environmental effects on minority or low-income populations because it increases the level of environmental protection for all affected populations without having any disproportionately high and adverse human health or environmental effects on any population, including any minority or low-income population.

XXVI. Congressional Review Act

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, generally provides that before a rule may take effect, the Agency promulgating the rule must submit a rule report to each House of the Congress and the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This rule is not a “major rule” as defined by 5 U.S.C. 804(2).

List of Subjects

40 CFR Part 158

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

40 CFR Part 161

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: April 19, 2013.

Bob Perciasepe,

Acting Administrator.

Therefore, under the authority of 7 U.S.C. 136-136y and 21 U.S.C. 346a, 40 CFR Chapter I is amended as follows:

PART 158 — [AMENDED]

1. The authority citation for part 158 continues to read as follows:

Authority: 7 U.S.C. 136-136y and 21 U.S.C. 346a.

2. Revise § 158.1(c)(4) to read as follows:

§ 158.1 Purpose and scope.

* * * * *

(c) * * *

(4) *Antimicrobial pesticides.* Subparts A, B, C, D, and W of this part apply to antimicrobial pesticides.

3. In § 158.100 revise the heading of paragraph (a); revise paragraph (b); redesignate paragraph (c) as paragraph (e); revise newly redesignated paragraph (e) and add new paragraphs (c) and (d), to read as follows:

§ 158.100 Pesticide use patterns.

(a) *General use patterns for conventional, biochemical, and microbial pesticides.****

(b) *Pesticide use site index for conventional, biochemical, and microbial pesticides.* The Pesticide Use Site Index for Conventional, Biochemical, and Microbial Pesticides is a comprehensive list of specific pesticide use sites. The index is alphabetized separately by site for all agricultural and all nonagricultural uses. The Pesticide Use Site Index associates each pesticide use site with one or more of the 12 general use patterns. It may be used in conjunction with the data tables to determine the applicability of data requirements to specific uses. The Pesticide Use Site Index for Conventional, Biochemical, and Microbial Pesticides will be updated periodically, and is available from

the Agency or may be obtained from the Agency's website at

<http://www.epa.gov/pesticides>.

(c) *Antimicrobial pesticide use patterns*. The general use patterns for antimicrobial pesticides are described in § 158.2201.

(d) *Pesticide use site index for antimicrobial pesticides*. The Pesticide Use Site Index for Antimicrobial Pesticides is a comprehensive list of specific antimicrobial use sites. The index is alphabetized by antimicrobial use sites, and associates each antimicrobial use site with one or more of the antimicrobial use patterns. It may be used in conjunction with the data tables to determine the applicability of data requirements to specific uses. The Pesticide Use Site Index for Antimicrobial Pesticides will be updated periodically, and is available from the Agency or may be obtained from the Agency's website at <http://www.epa.gov/pesticides>.

(e) *Determination of use pattern*. Applicants unsure of the correct use pattern for their particular product should consult the Agency.

§158.400 [Amended]

4. In the table in § 158.400(d) remove the heading "Efficacy of Antimicrobial Agents," and the entries 91-2 through 91-8 under that category.

5. Add subpart W to read as follows:

Subpart W--Antimicrobial Pesticide Data Requirements

Sec.

158.2200 Applicability.

158.2201 Antimicrobial use patterns.

158.2203 Definitions.

158.2204 Public health and nonpublic health claims.

158.2210 Product chemistry.

158.2220 Product performance.

158.2230 Toxicology.

158.2240 Nontarget organisms.

158.2250 Nontarget plant protection.

158.2260 Applicator exposure.

158.2270 Post-application exposure.

158.2280 Environmental fate.

158.2290 Residue chemistry.

Subpart W--Antimicrobial Pesticide Data Requirements

§ 158.2200 Applicability.

Part 158, subpart W establishes data requirements for any pesticide product that is:

(a) A pesticide that is intended for use as an “antimicrobial pesticide” within the meaning of FIFRA sec. 2(mm)(1)(A), regardless of whether it also meets the criterion of FIFRA sec. 2(mm)(1)(B). That criterion excludes from the definition any antimicrobial product that is intended for a food-use requiring a tolerance or exemption under FFDCA sec. 408 or a food additive regulation or clearance under FFDCA sec. 409. EPA will apply this subpart to all products intended for an antimicrobial use, purpose or function; the exclusion in FIFRA sec. 2(mm)(1)(B) does not exclude products from the data requirements of this subpart.

(b) A product that bears both antimicrobial and non-antimicrobial uses or claims. Such a product is subject to the data requirements for pesticides in subparts C through O, and U or V of this part with respect to its non-antimicrobial uses and claims, and to the requirements of this subpart with respect to its antimicrobial uses and claims.

(c) A wood preservative, including a product that is intended to prevent wood degradation problems due to fungal rot or decay, sapstain, or molds.

(d) An antifoulant, including a product that is intended to kill or repel organisms that can attach to underwater surfaces, such as boat bottoms.

§ 158.2201 Antimicrobial use patterns.

(a) *Antimicrobial use patterns.* The 12 general use patterns used in the data tables in this subpart are:

- (1) Agricultural premises and equipment.
- (2) Food-handling/storage establishments, premises and equipment.
- (3) Commercial, institutional and industrial premises and equipment.
- (4) Residential and public access premises.
- (5) Medical premises and equipment.
- (6) Human drinking water systems.
- (7) Materials preservatives.
- (8) Industrial processes and water systems.
- (9) Antifoulant paints and coatings.
- (10) Wood preservatives.
- (11) Swimming pools.
- (12) Aquatic areas.

(b) *Use site index.* The Pesticide Use Site Index for Antimicrobial Pesticides is a comprehensive list of specific antimicrobial use sites. The Index associates antimicrobial use sites with one or more of the 12 antimicrobial use patterns. It is to be used in conjunction with the data tables in this subpart to determine the applicability of data requirements to specific uses. The Antimicrobial Pesticide Use Site Index, which will be updated periodically, is available from the Agency or may be obtained from the Agency's website at <http://www.epa.gov/pesticides>.

§ 158.2203 Definitions.

The following terms are defined for the purposes of this subpart:

Disinfectant means a substance, or mixture of substances, that destroys or irreversibly inactivates bacteria, fungi and viruses, but not necessarily bacterial spores, in

the inanimate environment.

Fungicide means a substance, or mixture of substances, that destroys fungi (including yeasts) and fungal spores pathogenic to man or other animals in the inanimate environment.

Microbiological water purifier means any unit, water treatment product or system that removes, kills or inactivates all types of disease-causing microorganisms from the water, including bacteria, viruses and protozoan cysts, so as to render the treated water safe for drinking.

Sanitizer means a substance, or mixture of substances, that reduces the bacteria population in the inanimate environment by significant numbers, but does not destroy or eliminate all bacteria. Sanitizers meeting Public Health Ordinances are generally used on food contact surfaces and are termed sanitizing rinses.

Sterilant means a substance, or mixture of substances, that destroys or eliminates all forms of microbial life in the inanimate environment, including all forms of vegetative bacteria, bacterial spores, fungi, fungal spores, and viruses.

Tuberculocide means a substance, or mixture of substances, that destroys or irreversibly inactivates tubercle bacilli in the inanimate environment.

Virucide means a substance, or mixture of substances, that destroys or irreversibly inactivates viruses in the inanimate environment.

§ 158.2204 Public health and nonpublic health claims.

(a) *Public health claim.* An antimicrobial pesticide is considered to make a public health claim if the pesticide product bears a claim to control pest microorganisms that pose a threat to human health, and whose presence cannot readily be observed by the user, including but not limited to, microorganisms infectious to man in any area of the inanimate environment. A product makes a public health claim if one or more of the following apply:

(1) A claim is made for control of specific microorganisms that are directly or indirectly infectious or pathogenic to man (or both man and animals). Examples of specific microorganisms include, but are not limited to: *Mycobacterium tuberculosis*, *Pseudomonas aeruginosa*, *Escherichia coli* (*E. coli*), *human immunodeficiency virus* (*HIV*), *Streptococcus*, and *Staphylococcus aureus*. Claims for control of microorganisms infectious or pathogenic only to animals (such as canine distemper virus or hog cholera virus) are not considered public health claims.

(2) A claim is made for the pesticide product as a sterilant, disinfectant, virucide, sanitizer, or tuberculocide against microorganisms that are infectious or pathogenic to man.

(3) A claim is made for the pesticide product as a fungicide against fungi infectious or pathogenic to man, or the product does not clearly state that it is intended for use only against nonpublic health fungi.

(4) A claim is made for the pesticide product as a microbiological water purifier or microbial purification system.

(5) A non-specific claim is made that the pesticide product will beneficially impact or affect public health at the site of use or in the environment in which it is applied, and:

(i) The pesticide product contains one or more ingredients that, under the criteria in 40 CFR 153.125(a), is an active ingredient with respect to a public health microorganism and there is no other functional purpose for the ingredient in the product; or

(ii) The pesticide product is similar in composition to a registered pesticide product that makes antimicrobial public health claims.

(b) *Nonpublic health claim.* An antimicrobial pesticide is considered to make a nonpublic health claim if the pesticide product bears a claim to control microorganisms of economic or aesthetic significance, where the presence of the microorganism would not normally lead to infection or disease in humans. Examples of nonpublic health claims include, but are not limited to: Algacides, slimicides, preservatives and products for

which a pesticidal claim with respect to odor sources is made.

§158.2210 Product chemistry.

The product chemistry data requirements of subpart D of this part apply to antimicrobial products covered by this subpart.

§158.2220 Product performance.

(a) *General.* (1) *Product performance requirement for all antimicrobial pesticides.* Each applicant must ensure through testing that his product is efficacious when used in accordance with label directions and commonly accepted pest control practices. The Agency may require, on a case-by-case basis, submission of product performance data for any pesticide product registered or proposed for registration or amendment.

(2) *Product performance data for each product that bears a public health claim.* Each product that bears a public health claim, as described in §158.2204(a), must be supported by product performance data, as listed in the table in paragraph (c) of this section. Product performance data must be submitted with any application for registration or amended registration.

(3) *Product performance data for each product that bears a nonpublic health claim.* Each product that bears a nonpublic health claim, as described in §158.2204(b), must be supported by product performance data. Each registrant must ensure through testing that his product is efficacious when used in accordance with label directions and commonly accepted practices. The Agency reserves the right to require, on a case-by-case basis, submission of product performance data for any pesticide product registered or proposed for registration or amendment.

(4) *Determination of data requirements.* Subpart B of this part and §158.2201 describe how to use the table in paragraph (c) of this section to determine the product performance data requirements for antimicrobial pesticide products.

(b) *Key.* R = Required; EP = End-use product.

(c) *Antimicrobial product performance data requirements table.* The following table shows the data requirements for antimicrobial product performance.

TABLE —ANTIMICROBIAL PRODUCT PERFORMANCE DATA REQUIREMENTS

Guideline Number	Data Requirement	All Use Patterns	Test Substance
810.2100	Sterilants – Efficacy Data Recommendations	R	EP
810.2200	Disinfectants for Use on Hard Surfaces – Efficacy Data Recommendations	R	EP
810.2300	Sanitizers for Use on Hard Surfaces – Efficacy Data Recommendations	R	EP
810.2400	Disinfectants and Sanitizers for Use on Fabrics and Textiles -- Efficacy Data Recommendations	R	EP
810.2500	Air Sanitizers – Efficacy Data Recommendations	R	EP
810.2600	Disinfectants for Use in Water -- Efficacy Data Recommendations	R	EP

§158.2230 Toxicology.

(a) *General.* Subpart B of this part and § 158.2201 describe how to use the table in paragraph (g) of this section to determine the toxicology data requirements for an antimicrobial pesticide product. Notes that apply to an individual test, including specific conditions, qualifications, or exceptions are listed in paragraph (h) of this section.

(b) *Uses.* The applicant for registration must first determine whether the use is likely to result in pesticide residues in food or water and therefore consult the “Food Use” columns of the table in paragraph (g) of this section. Generally, if the residues of the antimicrobial result from an application to a surface or if incorporated into a material that may come into contact with food or feed, and residues may be expected to transfer to such food or feed, then the “Indirect Food Uses” columns is to be consulted.

(c) *Tiering of data requirements.* Applicants for registration of antimicrobials may perform tests in a tiered fashion. After the initially required tests are conducted, additional testing may be required if results of the initial tests trigger the need for additional data.

Conditions that trigger the need for additional data are given in the test notes in paragraph (h) of this section.

(d) *200 parts per billion (ppb)*. The 200 ppb level was originally used by the Food and Drug Administration with respect to the concentration of residues in or on food for tiering of data requirements for indirect food use biocides. The Agency has also adopted this same residue level for determining toxicology data requirements for indirect food uses of antimicrobial pesticides. The 200 ppb level is the concentration of antimicrobial residues in or on the food item.

(e) *Use of OSHA standards*. If EPA determines that industrial standards, such as the workplace standards set by the Occupational Safety and Health Administration (OSHA standards), provide adequate protection for a particular pesticide or a particular use pattern, additional toxicity data may not be required for that pesticide or the use pattern.

(f) *Key*. R = Required; CR = Conditionally required; NR = Not required; MP = Manufacturing-use product; EP = End-use product; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product; PAI = Pure active ingredient; PAIRA = Pure active ingredient, radiolabeled; Choice = choice of several test substances depending on studies required.

(g) *Antimicrobial toxicology data requirements table*. The following table shows the data requirements for toxicology. The test notes applicable to the data requirements in this table appear in paragraph (h) of this section.

TABLE —ANTIMICROBIAL TOXICOLOGY DATA REQUIREMENTS

Guideline Number	Data Requirement	Food Uses			Nonfood Uses		Test Substance		Test Note No.
		Direct Food Uses	Indirect Food Uses (> 200 ppb)	Indirect Food Uses (≤ 200 ppb)	Swimming Pools, Aquatic Areas, Wood Preservatives, Metal Working Fluids	All Other Nonfood Uses	MP	EP	
Acute Testing									
870.1100	Acute oral toxicity – rat	R	R	R	R	R	MP and TGAI	EP and TGAI	1, 2
870.1200	Acute dermal toxicity	R	R	R	R	R	MP and TGAI	EP and TGAI	1, 2, 3
870.1300	Acute inhalation toxicity - rat	R	R	R	R	R	MP and TGAI	EP and TGAI	2, 4
870.2400	Primary eye irritation - rabbit	R	R	R	R	R	MP and TGAI	EP and TGAI	1, 2, 3
870.2500	Primary dermal irritation	R	R	R	R	R	MP and TGAI	EP and TGAI	1, 2, 3
870.2600	Dermal sensitization	R	R	R	R	R	MP and TGAI	EP and TGAI	1, 2, 3, 5
870.6200	Acute neurotoxicity - rat	R	R	CR	R	CR	TGAI	TGAI	6, 11
Subchronic Testing									
870.3100	90-Day oral toxicity - rodent	R	R	R	R	CR	TGAI	TGAI	8, 9, 15, 38
870.3150	90-Day oral toxicity - nonrodent	R	R	CR	R	CR	TGAI	TGAI	10, 15
870.3200	21/28-Day dermal toxicity	CR	CR	CR	CR	CR	TGAI	EP and TGAI	12, 13
870.3250	90-Day dermal toxicity	CR	CR	CR	CR	CR	TGAI	EP and TGAI	7, 13, 14, 15
870.3465	90-Day inhalation - toxicity - rat	CR	CR	CR	CR	CR	TGAI	TGAI	7, 15, 16, 17
870.6200	90-Day neurotoxicity - rat	R	R	CR	R	CR	TGAI	TGAI	6, 8
Chronic Testing									
870.4100	Chronic oral toxicity -	R	R	CR	R	CR	TGAI	TGAI	18, 19, 20

Guideline Number	Data Requirement	Food Uses			Nonfood Uses		Test Substance		Test Note No.
		Direct Food Uses	Indirect Food Uses (> 200 ppb)	Indirect Food Uses (≤ 200 ppb)	Swimming Pools, Aquatic Areas, Wood Preservatives, Metal Working Fluids	All Other Nonfood Uses	MP	EP	
	rodent								
870.4200	Carcinogenicity – two rodent species – rat and mouse preferred	R	R	CR	R	CR	TGAI	TGAI	19, 21, 22
Developmental Toxicity and Reproduction									
870.3700	Prenatal developmental toxicity - rat and rabbit preferred	R	R	R	R	R	TGAI	TGAI	23, 24, 25, 26
870.3800	Reproduction and fertility effects	R	R	R	R	R	TGAI	TGAI	26, 27, 28, 29
870.6300	Developmental neurotoxicity	CR	CR	CR	CR	CR	TGAI	TGAI	28, 29, 30
Mutagenicity									
870.5100	Reverse mutation assay	R	R	R	R	R	TGAI	TGAI	31, 32
870.5300 870.5375	<i>In vitro</i> mammalian gene mutation	R	R	R	R	R	TGAI	TGAI	31, 33
870.5385 870.5395	<i>In vivo</i> cytogenetics	R	R	R	R	R	TGAI	TGAI	31, 34
Special Testing									
870.7485	Metabolism and pharmacokinetics	R	R	CR	R	CR	PAI or PAIRA	PAI or PAIRA	35, 39
870.7200	Companion animal safety	CR	CR	CR	CR	CR	NR	Choice	36
870.7600	Dermal penetration	CR	CR	CR	CR	CR	Choice	Choice	3, 37
870.7800	Immunotoxicity	R	R	R	R	R	TGAI	TGAI	8

(h) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (g) of this section:

1. Not required if test material is a gas or highly volatile liquid.
2. The six end-use product (EP) acute toxicity studies are required using the product as formulated for sale and distribution. In addition, if the EP label has directions for diluting the product, then, the applicant may also need to conduct certain of the acute toxicity studies using the highest concentration labeled for dilution (i.e., the least diluted product). The end-use dilution testing is in addition to the testing conducted on the EP.
3. Not required if test material is corrosive to skin or has pH less than 2 or greater than 11.5.
4. Data are required when the product consists of, or under conditions of use will result in, a respirable material (e.g., gas, vapor, aerosol or particulates).
5. Data are required if repeated dermal exposure is likely to occur under conditions of use.
6. For indirect food uses ≤ 200 ppb, and all other nonfood uses, data are required if the neurotoxicity screen in the 90-day oral rodent study or other data indicate neurotoxicity.
7. The 90-day dermal toxicity study and/or 90-day inhalation toxicity study are required if the Agency determines that dermal and/or inhalation exposure is the primary route of exposure.
8. All 90-day subchronic studies in the rodent can be designed to simultaneously fulfill the requirements of the 90-day neurotoxicity and/or immunotoxicity studies by adding separate groups of animals for testing of neurotoxicity and/or immunotoxicity parameters.
9. The 90-day study is required in the rodent for hazard characterization (possibly endpoint selection) and dose-setting for the chronic/carcinogenicity study. It is not required in the mouse, but the Agency would encourage the applicant to conduct a 90-day range finding study for the purposes of dose selection for the mouse carcinogenicity study to achieve adequate dosing and an acceptable study.
10. A 1-year non-rodent study (i.e., 1-year dog study) may be required if the Agency finds that a pesticide chemical is highly bioaccumulative and slowly eliminated. EPA may also require the appropriate metabolism and pharmacokinetic studies to evaluate more precisely bioavailability, half life, and steady state to determine if a longer duration dog toxicity study is needed.
11. Although the subchronic toxicity testing guidelines include measurement of neurological endpoints, such screens do not meet the requirement of the 90-day neurotoxicity study. For nonfood uses, if the 90-day study does not include a neurotoxicity screen, then the acute neurotoxicity study will be required.
12. Data are required if all of the following criteria are met:
 - i. The intended use of the antimicrobial pesticide product is expected to result in repeated dermal human exposure to the product.
 - ii. Data from a 90-day dermal toxicity study are not available.
 - iii. The 90-day dermal toxicity study has not been triggered.
13. EP testing is required if the product or any component of the product may increase dermal absorption of the active ingredient(s) or increases its toxic or pharmacologic effects, as determined by testing using the TGAI or based on available information about the toxic effects of the product or its components.
14. Data are required if the active ingredient in the product is known or expected to be metabolized differently by the dermal route of exposure than by the oral route, and a metabolite of the active ingredient is the toxic moiety.
15. A 90-day oral toxicity test is not required for heating, ventilation, air conditioning, and refrigeration systems (collectively referred to as HVAC&R). Instead, two 90-day toxicity tests, one by the dermal route and one by the inhalation route are required.
16. Data are required if there is the likelihood of significant repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol.
17. Based on estimates of the magnitude and duration of human exposure, studies of shorter duration, e.g., 21- or 28-days, may be sufficient to satisfy this requirement. The prime consideration in determining the appropriateness of a shorter duration study is the likely period of time for which humans will be exposed.
18. Based on the positive results of the acute or 90-day neurotoxicity studies, or on other data indicating neurotoxicity, a chronic neurotoxicity study (i.e., a chronic study with additional neurotoxicity evaluations) may be required to provide information about potential neurotoxic effects from long-term exposures.
19. Studies which are designed to simultaneously fulfill the requirements of both the chronic oral and carcinogenicity studies (i.e., a combined study) may be conducted.

20. For indirect food uses ≤ 200 ppb, and all other nonfood uses, data are required if either of the following criteria are met:
 - i. The use of the pesticide is likely to result in repeated human exposure over a considerable portion of the human lifespan; or
 - ii. The use requires that a tolerance, tolerance exemption, or food additive regulation or clearance be established.
21. For indirect food uses ≤ 200 ppb, and all other nonfood uses, data are required if any of the following criteria, are met:
 - i. The use of the pesticide is likely to result in significant human exposure over a considerable portion of the human life span which is significant in terms of frequency, time, duration, and/or magnitude of exposure.
 - ii. The use requires that a tolerance, tolerance exemption, or food additive regulation or clearance be established.
 - iii. The active ingredient, metabolite, degradate, or impurity:
 - A. Is structurally related to a recognized carcinogen;
 - B. Causes mutagenic effects as demonstrated by *in vitro* or *in vivo* testing; or
 - C. Produces a morphologic effect in any organ (e.g., hyperplasia, metaplasia) in subchronic studies that may lead to a neoplastic change.
22. If the requirement for a carcinogenicity study in any species is modified or waived for any reason, then a subchronic 90-day oral study in the same species may be required.
23. Testing in two species is required for all uses.
24. The oral route, by oral intubation, is preferred, unless the chemical or physical properties of the test substance, or the pattern of human exposure, suggest a more appropriate route of exposure.
25. Additional testing by other routes of exposure may be required if the pesticide is determined to be a prenatal developmental toxicant after oral dosing.
26. The developmental toxicity study in rodents may be combined with the two-generation reproduction study in rodents by using a second mating of the parental animals in either generation. Protocols must be approved by the Agency prior to the initiation of the study.
27. A two-generation reproduction study is required.
28. An information-based approach to testing is preferred, which utilizes the best available knowledge on the chemical (hazard, pharmacokinetic, or mechanistic data) to determine whether a standard guideline study, an enhanced guideline study, or an alternative study should be conducted to assess potential hazard to the developing animal. Applicants must submit any alternative proposed testing protocols and supporting scientific rationale to the Agency. Protocols must be approved by the Agency prior to the initiation of the study.
29. The use of a combined two-generation reproduction/developmental neurotoxicity study that utilizes the two-generation reproduction study in rodents as a basic protocol for the addition of other endpoints or functional assessments in the immature animal is encouraged.
30. A DNT study is required using a weight-of-evidence approach when:
 - i. The pesticide causes treatment-related neurological effects in adult animal studies (i.e., clinical signs of neurotoxicity, neuropathology, functional or behavioral effects).
 - ii. The pesticide causes treatment-related neurological effects in developing animals, following pre- or post-natal exposure (i.e., nervous system malformations or neuropathy, brain weight changes in offspring, functional or behavioral changes in the offspring).
 - iii. The pesticide elicits a causative association between exposures and adverse neurological effects in human epidemiological studies.
 - iv. The pesticide evokes a mechanism that is associated with adverse effects on the development of the nervous system (i.e., structure-activity-relationship (SAR) to known neurotoxicants, altered neuroreceptor or neurotransmitter responses).
31. To facilitate the weight-of-evidence determination for the pesticide's mutagenicity, in addition to those specifically listed in this table, the Agency requires submission of other mutagenicity test results that may have been performed. A reference list of all studies and papers known to the applicant concerning the mutagenicity of the test chemical must be submitted with the required studies.
32. Due to the nature of antimicrobials, if testing with bacterial strains has not been conducted, then testing using a mammalian cell assay such as the mouse lymphoma TK +/- assay is preferred. If reverse mutation assay testing with bacterial strains has already been conducted, and the testing was conducted at levels that did not cause toxicity to the bacterial strains tested, then the applicant may submit the study to fulfill this data requirement.

33. For the *in vitro* mammalian gene mutation study, there is a choice of assays using either mouse lymphoma L5178Y cell thymidine kinase (tk) gene locus, maximizing assay conditions for small colony expression and detection; Chinese hamster ovary (CHO) or Chinese hamster lung fibroblast (v79) cells, hypoxanthine-guanine phosphoribosyl transferase (hgp_{rt}) gene locus, accompanied by an appropriate *in vitro* test for clastogenicity; or CHO cells strains AS52, xanthine-guanine phosphoribosyl transferase (xp_{rt}) gene locus.

34. There is a choice of assays, but the micronucleus rodent bone marrow assay is preferred; the rodent bone marrow assays using metaphase analysis (aberrations) are acceptable.

35. Data are required when chronic toxicity or carcinogenicity studies are also required.

36. Data is required if the product label directs that it be applied to domestic animals, such as cats, dogs, cattle, pigs, and horses.

37. In the absence of dermal absorption data or a repeated dose dermal toxicity study, the assumption of 100 percent dermal absorption would be used in a risk assessment to determine if a dermal penetration study is required, and to identify the doses and duration of exposure for which dermal absorption is to be quantified.

38. Required for nonfood uses, if oral exposure could occur.

39. Data may be required if significant adverse effects are seen in available toxicology studies and these effects can be further elucidated by metabolism and pharmacokinetics studies.

§ 158.2240 Nontarget organisms.

(a) *General.* Subpart B of this part and § 158.2201 describe how to use the table in paragraph (c) of this section to determine the terrestrial and aquatic nontarget organisms data requirements for a particular antimicrobial pesticide product. Notes that apply to an individual test, including specific conditions, qualifications, or exceptions are listed in paragraph (d) of this section.

(1) Terrestrial and aquatic nontarget organism data are required to support the registration of most end-use and manufacturing-use antimicrobial products.

(2) Data are generally not required to support end-use products of a gas, highly volatile liquid, highly reactive solid, or a highly corrosive material.

(3) Data on transformation/degradation products or leachate residues of the parent compound are also required to support registration, if the transformation/degradation/degradation products or leachate residues meet one of the following criteria:

- (i) More toxic, persistent, or bioaccumulative than the parent;
- (ii) Have been shown to cause adverse effects in mammalian or aquatic reproductive studies; or
- (iii) The moiety of concern (i.e., functional group in the parent chemical molecule

that imparts adverse effects) remains intact.

(4) If an antimicrobial may be applied to a field crop, horticultural crop, or turf, then the data requirements in §158.630 apply.

(5) For the purpose of determining data requirements, the all other use patterns category includes the following use patterns:

- (i) Agricultural premises and equipment.
- (ii) Food-handling/storage establishments, premises, and equipment.
- (iii) Commercial, institutional and industrial premises and equipment.
- (iv) Residential and public access premises.
- (v) Medical premises and equipment.
- (vi) Human drinking water systems.
- (vii) Materials preservatives.
- (viii) Swimming pools.

(b) *Key.* MP = Manufacturing use product; EP = End-use product; R = Required; CR = Conditionally required; NR = Not required; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product; PAIRA = Pure active ingredient radiolabeled; a.i. = active ingredient.

(c) *Antimicrobial nontarget organism data requirements table.* The following table shows the data requirements for nontarget organisms. The test notes appear in paragraph (d) of this section.

TABLE — ANTIMICROBIAL NONTARGET ORGANISM DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern					Test Substance		Test Note No.
		Industrial Processes and Water Systems	Antifoulant Coatings and Paints	Wood Preservatives	Aquatic Areas	All Other Use Patterns Category	MP	EP	
Tier One Testing									
850.2100	Acute avian oral toxicity	R	R	R	R	R	TGAI	TGAI	1
850.1010	Acute freshwater invertebrates toxicity	R	R	R	R	R	TGAI	TGAI	2
850.1075	Acute freshwater fish toxicity	R	R	R	R	R	TGAI	TGAI	3
Higher Tier Testing									
Avian Testing									
850.2200	Avian dietary toxicity	CR	CR	CR	CR	CR	TGAI	TGAI	4
850.2300	Avian reproduction	CR	CR	CR	CR	CR	TGAI	TGAI	1, 6
Aquatic Organisms Testing									
850.1010	Acute freshwater invertebrates toxicity	CR	CR	CR	CR	CR	---	TEP	2, 5, 7
850.1075	Acute freshwater fish toxicity	CR	CR	CR	CR	CR	---	TEP	3, 5, 7
850.1025 850.1035 850.1045	Acute estuarine and marine organisms toxicity	CR	R	CR	CR	CR	TGAI	TGAI	8, 9
850.1055 850.1075	Acute estuarine and marine organisms toxicity	CR	CR	CR	CR	CR	---	TEP	5, 7, 8
850.1400	Fish early-life stage	R	R	R	R	R	TGAI	TGAI	10
850.1300 850.1350	Aquatic invertebrate life-cycle	R	R	R	R	R	TGAI	TGAI	10
850.1500	Fish life-cycle	CR	CR	CR	CR	CR	TGAI	TGAI	11, 12
850.1710 850.1730 850.1850	Aquatic organisms, bioavailability, biomagnification, toxicity tests	CR	CR	CR	CR	CR	TGAI, PAI, degradate	TGAI, PAI, degradate	13

Guideline Number	Data Requirement	Use Pattern					Test Substance		Test Note No.
		Industrial Processes and Water Systems	Antifoulant Coatings and Paints	Wood Preservatives	Aquatic Areas	All Other Use Patterns Category	MP	EP	
850.1950	Simulated or actual field testing for aquatic organisms	CR	CR	CR	CR	CR	TEP	TEP	14, 15, 16
Sediment Testing									
850.1735	Whole sediment; acute freshwater invertebrates	CR	CR	CR	CR	CR	TGAI	TGAI	15, 17
850.1740	Whole sediment; acute marine invertebrates	CR	CR	CR	CR	CR	TGAI	TGAI	15, 17, 19
None	Whole sediment; chronic invertebrates fresh-water and marine	CR	CR	CR	CR	CR	TGAI	TGAI	15, 18, 19
Insect Pollinator Testing									
850.3020	Honeybee acute contact	NR	NR	R	NR	CR	TGAI	TGAI	20
850.3030	Toxicity of residues to honeybees	NR	NR	R	NR	CR	TGAI	TEP or treated wood	20, 21

(d) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (c) of this section:

1. For industrial processes and water systems, antifoulant paints and coatings, wood preservatives, and aquatic areas, data are required for two avian species: one waterfowl species and one upland game bird species. For the all other use patterns category (as specified in § 158.2240(a)(5)), data are required for one avian species.
2. Data are required on one freshwater aquatic invertebrate species.
3. For the industrial processes and water systems, antifoulant paints and coatings, wood preservatives, and aquatic use pattern areas, data are required on two species of fish, one cold water species and one warm water species. For the all other use patterns category (as specified in § 158.2240(a)(5)), data are required on one species of fish, either one cold water species or one warm water species. Testing on a second species is required if the active ingredient or principal transformation products are stable in the environment and the LC₅₀ in the first species is less than or equal to 1 ppm or 1 mg/L.
4. Data are required on one avian species, either one waterfowl species or one upland game bird species, if the avian acute oral LD₅₀ (TGAI testing) is less than or equal to 100 mg/a.i./kg and a.i. residues or its principal transformation products are likely to occur in avian feed items. Data on the second species are required if the avian dietary LC₅₀ in the first species tested is less than or equal to 500 ppm a.i. in the diet.
5. If TEP testing cannot be conducted due to the physical characteristics of the test substance (for example, a paint), then the applicant should request a waiver.
6. Data are required if one or more of the following criteria are met:
 - i. Birds may be subjected to repeated or continued exposure to the pesticide or any of its transformation products, especially preceding or during the breeding season.
 - ii. The pesticide or any of its major metabolites or degradation products are stable in the environment to the extent that a potentially toxic amount may persist in avian feed.
 - iii. The pesticide or any of its major metabolites or degradation products are stored or accumulated in plant or animal tissues, as indicated by the octanol/water partition coefficient (K_{ow} is greater than or equal to 1,000), accumulation studies, metabolic release and retention studies, or as indicated by structural similarity to known bioaccumulative chemicals.
 - iv. Any other information, such as that derived from mammalian reproduction studies, indicates that reproduction in terrestrial vertebrates may be adversely affected by the anticipated use of the pesticide product.
7. TEP testing is required for any product which meets one or more of the following conditions:
 - i. When based on deterministic modeling results: If the Estimated Environmental Concentration (EEC) in the aquatic environment is equal to or greater than one-half the LC₅₀/EC₅₀ of the TGAI.
 - ii. When based on probabilistic modeling results: If the estimated 10th percentile 7Q10 Surface Water Concentration exceeds the acute concentration of concern (i.e., one-half the LC₅₀/EC₅₀).
 - iii. If an ingredient in the end-use product other than the active ingredient is expected to enhance the toxicity of the active ingredient or to cause toxicity to aquatic organisms.
 - iv. The end-use antimicrobial product will be applied directly into an aquatic environment.
8. Data are required on one estuarine/marine mollusk, one other estuarine/marine invertebrate, and one estuarine/marine fish species.
9. For the all other use patterns category (as specified in § 158.2240(a)(5)), industrial processes and water systems, wood preservatives, and aquatic areas, data are required if the pesticide residues from the parent compound and/or transformation products are likely to enter the estuarine/marine environment.
10. Testing must be conducted with the most sensitive organism (either freshwater or estuarine/marine vertebrates, or freshwater or estuarine/marine invertebrates), as determined from the results of the acute toxicity tests (acute EC₅₀ freshwater invertebrates; acute LC₅₀/EC₅₀ estuarine and marine organisms; acute freshwater fish LC₅₀).
11. Data are required on estuarine/marine species if the product is intended for direct application to the estuarine or marine environment, or the product is expected to enter this environment in significant concentrations because of its expected use or mobility patterns.
12. Data are required on freshwater species if the end-use product is intended to be applied directly to water, or is expected to be transported to water from the intended use site, and when one or more of the following conditions apply:
 - i. When based on deterministic modeling results: If the Estimated Environmental Concentration (EEC) in water is equal to or greater than 0.1 of the no-observed-adverse-effect concentration or no-observed-adverse-effect level (NOAEC/NOAEL) in the fish early-life stage or invertebrate life cycle tests.
 - ii. When based on probabilistic modeling results: If the estimated 10th percentile 7Q10 Surface

Water Concentration based on probabilistic modeling exceeds for 20 days or more the chronic concentration of concern (i.e., one-tenth the NOAEC or NOAEL) determined in the fish early-life stage or invertebrate life cycle tests.

- iii. If studies of other organisms indicate that the reproductive physiology of fish may be affected.
- 13. Not required when:
 - i. The octanol/water partition coefficients of the pesticide and its major degradates are less than 1,000;
 - ii. There are no potential exposures to fish and other nontarget aquatic organisms; or
 - iii. The hydrolytic half-life is less than 5 days at pH 5, 7, and 9.
- 14. Environmental chemistry methods used to generate data associated with this study must include results of a successful confirmatory method trial by an independent laboratory. Test standards and procedures for independent laboratory validation are available as addenda to the guideline for this test requirement.
- 15. Protocols must be approved by the Agency prior to the initiation of the study.
- 16. Data are required if the intended use pattern, and the physical/chemical properties and environmental fate characteristics of the antimicrobial indicate significant potential exposure, and, based on the results of the acute and chronic aquatic organism testing, significant impairment of nontarget aquatic organisms could result.
- 17. Data are required if the half-life of the pesticide in the sediment is equal to or less than 10 days in either the aerobic soil or aquatic metabolism studies, and if one or more of the following conditions are met:
 - i. The soil partition coefficient (K_d) is equal to or greater than 50 L/kg.
 - ii. The $\log K_{ow}$ is equal to or greater than 3.
 - iii. The K_{oc} is equal to or greater than 1,000.
- 18. Data are required if the EEC in sediment is greater than 0.1 of the acute LC_{50}/EC_{50} values and if one or more of the following conditions are met:
 - i. The soil partition coefficient (K_d) is equal to or greater than 50 L/kg.
 - ii. The $\log K_{ow}$ is equal to or greater than 3.
 - iii. The K_{oc} is equal to or greater than 1,000.
- 19. Sediment testing with estuarine/marine test species is required if the product is intended for direct application to the estuarine or marine environment or the product is expected to enter this environment in significant concentrations either by runoff or erosion, because of its expected use or mobility pattern.
- 20. For the all other use patterns category (as specified in § 158.2240(a)(5)), data are required only for beehive applications when the beehive (empty or occupied) may be treated.
- 21. A study similar to “Honey Bee Toxicity of Residues on Foliage” is required using treated wood instead of the foliage. Protocols must be approved by the Agency prior to the initiation of the study.

§158.2250 Nontarget plant protection.

- (a) Subpart B of this part and § 158.2201 describe how to use the table in paragraph (f) of this section to determine the nontarget plant protection data requirements for a particular antimicrobial pesticide product. Notes that apply to an individual test including specific conditions, qualifications, or exceptions are listed in paragraph (g) of this section.
- (b) Data on transformation/degradation products or leachate residues of the parent compound are also required to support registration, if the transformation/ degradation products or leachate residues meet one of the following criteria:

- (1) More toxic, persistent, or bioaccumulative than the parent;
- (2) Have been shown to cause adverse effects in mammalian or aquatic reproductive studies; or
- (3) The moiety of concern (i.e., functional group in the parent chemical molecule that imparts adverse effects) remains intact.

(c) For the purpose of determining data requirements, the all other use patterns category includes the following use patterns:

- (1) Agricultural premises and equipment.
- (2) Food-handling/storage establishments, premises, and equipment.
- (3) Commercial, institutional and industrial premises and equipment.
- (4) Residential and public access premises.
- (5) Medical premises and equipment.
- (6) Human drinking water systems.
- (7) Materials preservatives.
- (8) Swimming pools.

(d) If an antimicrobial may be applied to a field crop, horticultural crop, or turf, then the data requirements in § 158.660 apply.

(e) *Key.* MP = Manufacturing use product; EP = End-use product; R = Required; CR = Conditionally required; NR = Not required; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product.

(f) *Nontarget plant protection data requirements table.* The following table shows the data requirements for nontarget plant protection. The test notes appear in paragraph (g) of this section.

TABLE — NONTARGET PLANT PROTECTION DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern					Test Substance		Test Note No.
		Industrial Processes and Water Systems	Antifoulant Coatings and Paints	Wood Preservatives	Aquatic Areas	All Other Use Patterns Category			
							MP	EP	
850.4225	Seedling emergence, Tier II – dose response	CR	CR	CR	CR	CR	TEP	TEP	1, 2
850.4250	Vegetative vigor, Tier II – dose response	CR	NR	CR	CR	CR	TEP	TEP	1, 3
850.4400	Aquatic plant growth (aquatic vascular plant) Tier II – dose response	R	R	R	R	CR	TGAI, TEP	TGAI, TEP	4, 10
850.5400	Aquatic plant growth (algal) Tier II (dose response)	R	R	R	R	R	TGAI, TEP	TGAI, TEP	4, 5, 6
850.4300	Terrestrial field	CR	CR	CR	CR	CR	TEP	TEP	7, 8, 9
850.4450	Aquatic field	CR	CR	CR	CR	CR	TEP	TEP	7, 8, 9

(g) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (f) of this section:

1. Data on only one plant species (rice, *Oryza sativa*) are required.
2. Data are required if the risk quotient from any aquatic plant growth Tier II study exceeds a level of concern for aquatic plants.
3. Not required when:
 - i. There are no potential exposures to plants;
 - ii. The hydrolytic half-life is less than 5 days at pH 5, 7, and 9; or
 - iii. The results of a biodegradation study indicate that the active ingredient or principal degradation products are not biodegradable in 28 days, i.e., the biodegradation curve has not reached a plateau for at least three determinations within the 28 days.
4. For TEP testing, data are required for the applicant's end-use product if an ingredient in the end-use product, other than the active ingredient, is expected to enhance the toxicity of the active ingredient.
5. One Tier II (dose response) study, conducted with *Selenastrum capricornutum*, is required for the all other use patterns category (as specified in § 158.2250(c)). If the results of this study exhibit detrimental effects (EC_{50} less than 1.0 ppm or mg/L), then additional Tier II (dose response) studies are required on three species (*Anabaena flos-aquae*, *Navicula pelliculosa*, and *Skeletonema costatum*).
6. For industrial processes and water systems, antifoulant coatings and paints, wood preservatives, and aquatic areas, Tier II (dose response) studies are required on four species (*Anabaena flos-aquae*, *Navicula pelliculosa*, *Skeletonema costatum*, and *Selenastrum capricornutum*).
7. Environmental chemistry methods used to generate data must include the results of a successful confirmatory method trial by an independent laboratory.
8. Tests are required on a case-by-case basis based on the results of lower tier plant protection studies, adverse incident reports, intended use pattern, and environmental fate characteristics that indicate potential exposure.
9. Protocols must be approved by the Agency prior to the initiation of the study.
10. For the all other use patterns category (as specified in § 158.2250(c)), data are required if the aquatic (algal) plant growth Tier II study demonstrates detrimental effects at less than 1.0 ppm or mg/L.

§158.2260 Applicator exposure.

(a) *General.* Subpart B of this part and § 158.2201 describe how to use the table in paragraph (d) of this section to determine the applicator exposure data requirements for antimicrobial pesticide products. Notes that apply to an individual test including specific conditions, qualifications, or exceptions are listed in paragraph (e) of this section.

(1) The Agency may accept surrogate exposure data estimations and/or modeling estimations from other sources to satisfy exposure data requirements. The surrogate data must meet the basic quality assurance, quality control, good laboratory practice, and other scientific requirements set by EPA. To be acceptable, the Agency must find that the

surrogate exposure data estimations have adequate information to address the applicable exposure data requirements and contain adequate monitoring events of acceptable quality. The data must reflect the specific use prescribed on the label and the activity of concern, including formulation type, application methods and rates, type of activity, and other pertinent information.

(2) Occupational uses include not only handlers, mixers, loaders, and applicators, but also commercial applications to residential sites. Residential uses are limited to non-occupational, i.e., non-professional, antimicrobial applications. Both occupational and residential applicator data may be required for the same product.

(b) *Criteria for testing.* Applicator exposure data described in the table to paragraph (d) of this section are required based on toxicity and exposure criteria. Data are required if at least one of the toxicity criteria in paragraph (b)(1) of this section, and at least one of the exposure criteria in paragraph (b)(2) of this section are met.

(1) *Toxicity criteria.* (i) Evidence of potentially significant adverse effects have been observed in any applicable toxicity studies.

(ii) Scientifically sound epidemiological or poisoning incident data with a clear cause-effect relationship indicating that adverse health effects may have resulted from exposure to the pesticide.

(2) *Exposure criteria.* (i) Dermal exposure may occur during product use.

(ii) Respiratory exposure may occur during product use.

(c) *Key.* R = Required; CR = Conditionally required; TEP = Typical end-use product.

(d) *Antimicrobial applicator exposure data requirements table.* The following table shows the data requirements for applicator exposure. The test notes appear in

paragraph (e) of this section.

TABLE — ANTIMICROBIAL APPLICATOR EXPOSURE DATA REQUIREMENTS

Guideline Number	Data Requirements	Use Sites		Test Substance	Test Note No.
		Occupational	Residential		
875.1100 875.1200	Dermal exposure	R	R	TEP	1, 2, 3, 4
875.1300 875.1400	Inhalation exposure	R	R	TEP	1, 2, 3, 4
875.1500	Biological monitoring	CR	CR	TEP	1, 2, 3
875.1600	Data reporting and calculations	R	R	TEP	5
875.1700	Product use information	R	R	TEP	--

(e) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (d) of this section:

1. Prior to initiation of the study, protocols involving intentional exposure of human subjects must be submitted for review by EPA and then the Human Studies Review Board (HSRB) according to 40 CFR 26.1125. Examples of proposed human study research can be found in various reviews provided by the Human Studies Review Board (<http://www.epa.gov/osa/hsrb/index.htm>).
2. Biological monitoring data may be submitted in addition to, or in lieu of, dermal and inhalation passive dosimetry exposure data, provided the human pharmacokinetics of the pesticide or metabolite/analog compounds (*i.e.*, whichever method is selected as an indicator of body burden or internal dose) allow for the back calculation to the total internal dose.
3. For products with both indoor and outdoor uses, and similar conditions of use, data are generally required for the indoor applications only. However, data for outdoor uses are required if the Agency expects outdoor uses to result in greater exposure than indoor uses (e.g., higher use rates and application frequency, or longer exposure duration, or application methods/equipment create potential for increased dermal or inhalation exposure in outdoor versus indoor use sites). In certain cases, when a pesticide may be used both indoors and outdoors under dissimilar conditions of use, the Agency may require submission of applicator exposure data for both use patterns.
4. EPA will consider waiving this data requirement for antimicrobials applied via closed loading systems if the antimicrobial has a low vapor pressure.
5. Data reporting and calculations are required only if handler exposure data are required.

§158.2270 Post-application exposure.

(a) *General.* Subpart B of this part and § 158.2201 describe how to use the table in paragraph (d) of this section to determine the post-application exposure data requirements for antimicrobial pesticide products. The data generated during these studies are used to determine the quantity of pesticide to which people may be exposed after application. Notes that apply to an individual test, including specific conditions, qualifications, or exceptions to the designated test, are listed in paragraph (e) of this section.

(1) Post-application exposure data are required when certain toxicity criteria are met and the human activities associated with the pesticide's use pattern can lead to

potential adverse exposures.

(2) The Agency may accept surrogate exposure data estimations and/or modeling estimations from other sources to satisfy exposure data requirements. The surrogate data must meet the basic quality assurance, quality control, good laboratory practice, and other scientific requirements set by EPA. To be acceptable, the Agency must find that the surrogate exposure data estimations have adequate information to address the applicable exposure data requirements and contain adequate monitoring events of acceptable quality. The data must reflect the specific use prescribed on the label and the activity of concern, including formulation type, application methods and rates, type of activity, and other pertinent information.

(b) *Criteria for testing.* Post-application exposure data described in the table to paragraph (d) of this section are required based on toxicity and exposure criteria. Data are required if at least one of the toxicity criteria in paragraph (b)(1) of this section, and at least one of the exposure criteria in paragraph (b)(2) of this section are met.

(1) *Toxicity criteria.* (i) Evidence of potentially significant adverse effects have been observed in any applicable toxicity studies.

(ii) Scientifically sound epidemiological or poisoning incident data with a clear cause-effect relationship indicating that adverse health effects may have resulted from exposure to the pesticide.

(2) *Exposure criteria--(i) Outdoor uses.* (A) Occupational human post-application or bystander exposure to residues of antimicrobial pesticides could occur as the result of, but is not limited to, worker reentry into treatment sites, clean-up and equipment maintenance tasks, handling wood preservative-treated wood, or other work-related activity.

(B) Residential human post-application or bystander exposure to residues of antimicrobial pesticides could occur following the application of antimicrobial pesticides to outdoor areas and spaces at residential sites, such as, but not limited to homes, daycare centers, and other public buildings.

(ii) *Indoor uses.* (A) Occupational human post-application or bystander exposure to pesticide residues could occur following the application of the antimicrobial pesticide to indoor spaces or surfaces.

(B) Residential human post-application or bystander exposure to pesticide residues could occur following the application of the antimicrobial pesticide to indoor spaces or surfaces at residential sites, such as, but not limited to homes, daycare centers, hospitals, schools, and other public buildings.

(c) *Key.* R = Required; CR = Conditionally required; NR = Not required; TEP = Typical end-use product.

(d) *Antimicrobial post-application exposure data requirements table.* The following table shows the data requirements for post-application exposure. The test notes appear in paragraph (e) of this section.

TABLE — ANTIMICROBIAL POST-APPLICATION EXPOSURE DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Sites		Test Substance	Test Note No.
		Occupational	Residential		
875.2200	Soil residue dissipation	CR	CR	TEP	2, 3
875.2300	Indoor surface residue dissipation	CR	R	TEP	3, 4, 5, 6
875.2400	Dermal exposure	CR	CR	TEP	1, 7, 8
875.2500	Inhalation exposure	CR	CR	TEP	1, 7, 8, 9
875.2600	Biological monitoring	CR	CR	TEP	1, 8
875.2700	Product use information	R	R	TEP	---
875.2800	Description of human activity	R	R	TEP	---
875.2900	Data reporting and calculations	R	R	TEP	10

(e) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (d) of this section:

1. Prior to initiation of the study, protocols involving intentional exposure of human subjects must be submitted for review by EPA and then the Human Studies Review Board (HSRB) according to 40 CFR 26.1125. Examples of proposed human study research can be found in various reviews provided by the

Human Studies Review Board (HSRB) (<http://www.epa.gov/osa/hsrb/index.htm>).

2. For residential wood preservative uses, data may be required if soil has the potential to be an important exposure pathway, and soil is in contact with or adjacent to treated wood, including but not limited to decks, play sets, and gazebos,

3. Protocols must be approved by the Agency prior to the initiation of the study.

4. For wood preservatives, data are required for treated wood surfaces where post-application contact with treated wood is anticipated.

5. For occupational uses, data are required if the pesticide may be applied to or around surfaces, and if the human activity data indicate that workers are likely to have post-application dermal contact with treated surfaces while participating in typical activities.

6. Data are required for residential use sites, schools, and daycare institutions. This includes but is not limited to the following: Residential and public access premises; material preservatives (including those used in residential products, including but not limited to clothing and plastic toys) and wood preservatives (when contact with treated wood is likely to occur).

7. Data are required for occupational and residential uses if the human activity data indicate the potential for post-application dermal and/or inhalation exposures while participating in typical activities and no acceptable modeling options are available.

8. Biological monitoring data may be submitted in addition to, or in lieu of, dermal and inhalation passive dosimetry exposure data provided the human pharmacokinetics of the pesticide or metabolite/analog compounds (*i.e.*, whichever method is selected as an indicator of body burden or internal dose) allow for a back-calculation to the total internal dose.

9. Data are required for occupational and residential uses if there is the potential for bystander exposure and the pesticide use could result in respirable and/or inhalable material (e.g., gas, vapor, aerosol, or particulates).

10. Data reporting and calculations are required only if post-application exposure data are required.

§158.2280 Environmental fate.

(a) *General.* Subpart B of this part and § 158.2201 describe how to use the table in paragraph (c) of this section to determine the environmental fate data requirements for antimicrobial pesticide products. Notes that apply to an individual test including specific conditions, qualifications, or exceptions are listed in paragraph (d) of this section.

(1) Environmental fate data are required to support the registrations of all end-use and manufacturing-use antimicrobial products.

(2) Data on transformation/degradation products or leachate residues of the parent compound are also required to support registration, if the transformation/ degradation products or leachate residues meet one of the following criteria:

(i) More toxic, persistent, or bioaccumulative than the parent;

(ii) Have been shown to cause adverse effects in mammalian or aquatic reproductive studies; or

(iii) The moiety of concern (*i.e.*, functional group in the parent chemical molecule

that imparts adverse effects) remains intact.

(3) For the purpose of determining data requirements, the all other use patterns category includes the following use patterns:

- (i) Agricultural premises and equipment.
- (ii) Food-handling/storage establishments, premises, and equipment.
- (iii) Commercial, institutional and industrial premises and equipment.
- (iv) Residential and public access premises.
- (v) Medical premises and equipment.
- (vi) Human drinking water systems.
- (vii) Materials preservatives.
- (viii) Swimming pools.

(b) *Key.* MP = Manufacturing use product; EP = End-use product; R = Required; CR = Conditionally required; NR = Not required; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product; PAIRA = Pure active ingredient radiolabeled; ROC = residue of concern.

(c) *Antimicrobial environmental fate data requirements table.* The following table shows the data requirements for environmental fate. The test notes appear in paragraph (d) of this section.

TABLE — ANTIMICROBIAL ENVIRONMENTAL FATE DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern					Test Substance		Test Note No.
		Industrial Processes and Water Systems	Antifoulant Coatings and Paints	Wood Preservatives	Aquatic Areas	All Other Use Patterns Category	MP	EP	
Degradation Studies – Laboratory									
835.2120	Hydrolysis	R	R	R	R	R	TGAI or PAIRA	TGAI or PAIRA	1
835.2240	Photodegradation in water	R	R	R	R	R	TGAI or PAIRA	TGAI or PAIRA	2
835.2410	Photodegradation in soil	NR	NR	R	NR	NR	TGAI or PAIRA	TGAI or PAIRA	10
Toxicity and Fate in Wastewater Systems									
850.6800 OECD 209	Activated Sludge, Respiration Inhibition Test	R	R	R	NR	R	TGAI	TGAI	21
835.1110	Activated Sludge Sorption Isotherm	CR	CR	CR	NR	CR	TGAI	TGAI	19, 20
835.3110	Ready Biodegradability	CR	CR	CR	NR	CR	TGAI	TGAI	3, 4, 18
835.3220	Porous Pot Study	CR	CR	CR	NR	CR	TGAI	TGAI	3, 18
835.3280	Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater	CR	CR	CR	NR	CR	TGAI	TGAI	3, 18
835.3240	Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units	CR	CR	CR	NR	CR	TGAI	TGAI	3, 18
Mobility Studies									
835.1230 835.1240	Leaching and adsorption/de-sorption	R	R	R	R	CR	TGAI or PAIRA	TGAI or PAIRA	5, 6
Metabolism Studies – Laboratory									
835.4100	Aerobic soil metabolism	CR	NR	R	CR	CR	TGAI or PAIRA	TGAI or PAIRA	7, 8, 9
835.4200	Anaerobic soil metabolism	NR	NR	R	NR	CR	TGAI or PAIRA	TGAI or PAIRA	5, 8
835.4300	Aerobic aquatic metabolism	R	R	R	R	CR	TGAI or PAIRA	TGAI or PAIRA	5, 8

Guideline Number	Data Requirement	Use Pattern					Test Substance		Test Note No.
		Industrial Processes and Water Systems	Antifoulant Coatings and Paints	Wood Preservatives	Aquatic Areas	All Other Use Patterns Category	MP	EP	
835.4400	Anaerobic aquatic metabolism	R	R	R	R	CR	TGAI or PAIRA	TGAI or PAIRA	5, 8
<u>Dissipation Studies – Field</u>									
835.6200	Aquatic (sediment)	CR	R	CR	R	CR	TEP	TEP	11, 12, 13
<u>Ground and Surface Water Monitoring</u>									
None	Monitoring of representative U.S. waters	CR	CR	CR	CR	CR	ROC	ROC	11, 14, 17
<u>Special Studies</u>									
None	Special leaching	NR	R	R	NR	NR	TGAI	TEP	15, 16

(d) *Test notes.* The following test notes apply to the data requirements in the table in paragraph (c) of this section:

1. For testing antifoulant paints and coatings, testing is to be performed separately with both sterile buffered distilled water and sterile synthetic seawater at pHs 5, 7, and 9.
2. Not required if:
 - i. The electronic absorption spectra, measured at pHs 5, 7 and 9, of the chemical and its hydrolytic products, if any, show no absorption or tailing between 290 and 800 nm, inclusive; or
 - ii. The results of the hydrolysis study at all three pHs (5, 7, and 9) demonstrates a half-life of less than 30 days.
3. The results of the activated sludge, respiration inhibition (ASRI) test determine which of the following tests are required: Ready biodegradability, porous pot, the biodegradation in activated sludge study as described in the “Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater,” or simulation test – aerobic sewage treatment: A. activated sludge units.
 - i. If the ASRI test EC_{50} is equal to or less than 20 mg/L, then the applicant must choose either to:
 - A. Conduct the biodegradation in activated sludge study as described in the “Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater”;
 - B. Conduct the porous pot test; or
 - C. Conduct the simulation test – aerobic sewage treatment: A. activated sludge units.
 - ii. If the ASRI test EC_{50} is greater than 20 mg/L, then the applicant must choose either to:
 - A. Conduct a ready biodegradability study; or
 - B. Conduct one of the following studies: The biodegradation in activated sludge study as described in the “Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater,” the porous pot test, or the simulation test – aerobic sewage treatment: A. activated sludge units.
4. Pass criteria for the ready biodegradability study are: 70 percent removal of dissolved organic carbon (DOC) and 60 percent removal of theoretical oxygen demand (ThOD) or theoretical carbon dioxide (ThCO₂) production for respirometric methods. These pass levels must be reached in a 10-day window within the 28-day period of the test. If the antimicrobial passes the ready biodegradability study, then no further testing is required. If the antimicrobial fails the ready biodegradability study, then the applicant must conduct one of the following studies: The biodegradation in activated sludge study as described in the “Simulation Tests to Assess the Biodegradability of Chemicals Discharged in Wastewater,” the porous pot test, or the simulation test – aerobic sewage treatment: A. activated sludge units.
5. For the all other use patterns category (as specified in § 158.2280(a)(3)), data are required based on a weight-of-evidence evaluation of the results of the hydrolysis, photodegradation in water, activated sludge sorption isotherm, biodegradability, and activated sludge, respiration inhibition tests.
6. Adsorption and desorption using a batch equilibrium method is preferred. In some cases, as when the antimicrobial pesticide degrades rapidly, soil column leaching with unaged or aged columns may be more appropriate to fully characterize the potential mobility of the parent compound and major transformation products.
7. For industrial processes and water systems, aquatic areas, and the all other use patterns category (as specified in § 158.2280(a)(3)), data are required based on a weight-of-evidence evaluation of the results of the hydrolysis, photodegradation in water, activated sludge sorption isotherm, biodegradability, and activated sludge, respiration inhibition tests.
8. The environmental media (soil, water, hydrosol, and biota) to be utilized in these studies must be collected from areas representative of potential use sites.
9. For industrial processes and water systems, and aquatic areas, data are required for use sites that are intermittently dry.
10. Data are not required if the antimicrobial is an inorganic substance or a metal salt; or if the standardized soil profiles demonstrate that the antimicrobial is likely to readily degrade either microbially or via redox reactions (chemically) and no transformation/degrade/leachate products of concern (as described under § 158.2280(a)(2)) are produced.
11. Analytical methods used to generate data associated with this study must include results of a successful confirmatory method trial by an independent laboratory.
12. Protocols must be approved by the Agency prior to the initiation of the study.
13. For industrial processes and water systems, wood preservatives, and the all other use patterns category (as specified in § 158.2280(a)(3)), data are required based on the potential for aquatic exposure and if the weight-of-evidence indicates that the active ingredient or principal transformation products are likely to have the potential for persistence, mobility, nontarget aquatic toxicity, or bioaccumulation.
14. Data are required if the weight-of-evidence indicates that the active ingredient or principal

transformation products are likely to occur in nontarget freshwater, estuarine, or marine waters such that human or environmental exposures are likely to occur. In making that determination, the Agency takes into account other factors such as the toxicity of the chemical(s), available monitoring data and the vulnerability of the freshwater, estuarine, or marine water resources in the antimicrobial use area.

15. For wood preservatives, an aquatic leaching study is required. A soil leaching study is required if human or environmental exposures are likely to occur from leachates that contain the active ingredient or principal transformation products from wood treated with a preservative product. Protocols must be approved by the Agency prior to the initiation of the study.

16. For antifoulant paints and coatings, a leaching study is required. Protocols must be approved by the Agency prior to the initiation of the study.

17. Protocols, which include the residues of concern (such as parent, degrade/transform product, and/or leachate residues) that would be monitored, must be approved by the Agency prior to the initiation of the study.

18. A biodegradation study is not required if the antimicrobial meets one or more of the following criteria:

- i. Classified as a metal,
- ii. Relatively volatile, but not hydrophobic,
- iii. Highly reactive,
- iv. Both the parent and all transformation/degrade products (as described under § 158.2280(a)(2)) have half-lives of less than 3 hours,
- v. None of the registered or proposed product uses would result in transport of the parent and its transformation/degrade products (as described under § 158.2280(a)(2)) to a wastewater treatment plant.

19. The activated sludge sorption isotherm test is not required if the antimicrobial is:

- i. Relatively volatile, but not hydrophobic;
- ii. Highly reactive; or
- iii. The $\log K_{ow}$ is less than 3.0.

20. If the criteria of test note 19 of this paragraph are not met, then the activated sludge sorption isotherm test is required if one or more of the following criteria are also met:

- i. The antimicrobial is a metal,
- ii. The $\log K_{ow}$ is greater than or equal to 3.0,
- iii. The antimicrobial is positively charged or polycationic,
- iv. The EC_{50} in the activated sludge, respiration inhibition test is less than or equal to 20 mg/L,
- v. The EC_{50} in the activated sludge, respiration inhibition test is greater than 20 mg/L, and the antimicrobial fails the ready biodegradability study.

21. The activated sludge respiration inhibition study is not required if none of the registered or proposed product uses would result in transport of the parent and its transformation/degrade products (as described under § 158.2280(a)(2)) to a wastewater treatment plant.

§ 158.2290 Residue chemistry.

(a) *General.* Subpart B of this part and §158.2201 describe how to use the table in paragraph (h) of this section to determine the residue chemistry data requirements for antimicrobial pesticide products. Notes that apply to an individual test including specific conditions, qualifications, or exceptions are listed in paragraph (i) of this section.

(b) Residue chemistry data are required for:

(1) Antimicrobial end-use products with uses that may result in residues in or on food, including but not limited to:

(i) Products that require a tolerance, tolerance exemption, or food additive

regulation or clearance.

(ii) Products that may be used to treat livestock or poultry drinking water, for food egg washing, or for fruit and vegetable rinses.

(iii) Products that may be applied to a surface or incorporated into a material that may contact food or feed. Data are required regardless of whether the antimicrobial is applied or impregnated for the purpose of imparting antimicrobial protection to external surfaces of the substance or article, or for the purpose of protecting the substance or article itself.

(iv) Products that may be applied to water that have the potential to result in residues in potable water, or in water used for livestock and poultry drinking water, irrigation of crops, or water containing fish that may be used for human food.

(v) Wood preservative or antifoulant products intended for treating submerged materials that may result in food contact (e.g., lobster pots, fish cages on fish farms).

(2) Each manufacturing-use product bearing directions for formulation into an end-use product bearing uses described in paragraph (b)(1) of this section.

(c) Residue chemistry data are not required under paragraph (b) of this section if no adverse effects (no toxicity endpoints) are associated with dietary exposure to the active ingredient or if theoretical (high-end) dietary exposure estimates combined with the applicable toxicity endpoint result in acute and chronic dietary risks that are below the Agency levels of concern.

(d) For purposes of this section, Magnitude of the Residue Studies include the following: Food-handling, migration studies, potable water, fish, irrigated crops, meat/milk/poultry/eggs, crop field trails, processed food or feed, and anticipated residues.

(e) If the antimicrobial chemical may be applied to a field crop, then the residue

chemistry data requirements of §158.1410 apply.

(f) The following term is defined for the purposes of this section:

Residue of concern means the parent pesticidal compound and its metabolites, degradates, and impurities of toxicological concern.

(g) *Key.* R = Required; CR = Conditionally required; NR = Not required; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product; PAI = Pure active ingredient; PAIRA = Pure active ingredient radiolabeled; ROC = Residue of concern.

(h) *Antimicrobial residue chemistry data requirements table.* The following table shows the data requirements for residue chemistry. The test notes appear in paragraph (i) of this section.

TABLE —ANTIMICROBIAL RESIDUE CHEMISTRY DATA REQUIREMENTS

Guideline Number	Data Requirement	Uses				Test Substance	Test Note No.
		Agricultural Premise	Indirect Food	Direct Food	Aquatic		
Supporting Information							
860.1100	Chemical identity	R	R	R	R	TGAI	--
860.1200	Directions for use	R	R	R	R	--	--
860.1550	Proposed tolerance/tolerance exemption	R	R	R	R	--	1
860.1560	Reasonable grounds in support of petition	R	R	R	R	--	1
860.1650	Submittal of analytical reference standards	R	R	R	R	PAI/ROC	2
Food-Contact Surfaces Or Impregnated Materials							
860.1460	Food-handling	CR	CR	CR	CR	TEP	3
None	Nature of residue on surfaces	CR	CR	CR	CR	PAIRA or TGAI	4
None	Migration studies	CR	CR	CR	CR	TEP	5
860.1340	Residue analytical method for data collection	CR	CR	CR	CR	ROC	6
860.1380	Storage stability	R	R	R	R	TEP or ROC	7
Higher tiered							
860.1300	Nature of the residue in plants	CR	CR	CR	CR	PAIRA	8
860.1300	Nature of the residue in livestock	CR	CR	CR	CR	PAIRA	9
860.1340	Residue analytical methods for tolerance/tolerance exemption enforcement	CR	CR	CR	CR	ROC	10
860.1360	Multiresidue method testing	CR	CR	CR	CR	ROC	11
860.1400	Potable water	CR	CR	CR	CR	TEP	12
860.1400	Fish	CR	CR	CR	CR	TEP	13
860.1400	Irrigated crops	CR	CR	CR	CR	TEP	14
860.1480	Meat/milk/poultry/eggs	CR	CR	CR	CR	TGAI or ROC	15
860.1500	Crop field trials	CR	CR	CR	CR	TEP	16
860.1520	Processed food or feed	CR	CR	CR	CR	TEP	17
None	Anticipated residues	CR	CR	CR	CR	ROC	18

(i) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (h) of this section:

1. A petition proposing a numerical tolerance or a tolerance exemption is required for any food or feed use subject to section 408 of FFDCA if the use is not covered by an existing tolerance or tolerance exemption. If the use is subject to FFDCA section 409, the applicant must identify to EPA an applicable section 409 food additive regulation or clearance, or submit a copy of a petition to FDA requesting a section 409 food additive regulation or clearance for the food or feed use.

2. An analytical reference standard is required for any food or feed use requiring a numeric tolerance or exemption. Material safety data sheets as specified by the Occupational Safety and Health Administration in 29 CFR 1910.1200 must accompany analytical standards.

3. Data are required if a pesticide may be used in a food-handling establishment unless data including, but not limited to, theoretical (high-end) estimates, radiolabeled laboratory data, or the nature of the residue on surfaces study show that residues will not occur in food or feed.

4. If an antimicrobial pesticide may be applied to a food-contact surface or impregnated into a food-contact material and if theoretical (high-end) estimates of exposure exceed EPA's risk level of concern, then the nature of the residue on surfaces study is required. Protocols must be approved by the Agency prior to the initiation of the study.

5. Based on the results of the nature of the residue on surfaces study, if residues of concern are identified, then the migration study will be required. Protocols must be approved by the Agency prior to the initiation of the study.

6. If a magnitude of the residue study, as specified in § 158.2290(d), is required, then a residue analytical method suitable for collecting data is also required. The method must be capable of determining all residues of concern, to permit calculation of dietary risk or to establish a tolerance or tolerance exemption.

7. If a magnitude of the residue study, as specified in § 158.2290(d), is required, then storage stability data are also required, unless analytical samples are stored for 30 days or less. If, during hazard characterization, a residue has been identified as "of concern" and is known to be volatile or labile, then storage stability data are required regardless of sample storage time.

8. If crop plants or metabolically active raw agricultural commodities of food crops may be directly or indirectly exposed to an antimicrobial, plant metabolism studies are required to determine the transformation products that may enter the human diet. Such exposure could include, but is not limited to:

- i. Treatment of storage or shipping containers,
- ii. Postharvest fruit and vegetable treatment prior to shipping or storage,
- iii. Use of antimicrobial-treated water for irrigation, and
- iv. Any direct food contact use.

9. If livestock may be exposed to an antimicrobial, then hen and ruminant metabolism studies are required to determine the identities of residues of concern that may enter the human diet from consumption of livestock commodities. Livestock may be exposed via the oral, dermal, or inhalation route following treatment or contamination of sites including, but not limited to, livestock premises, feed, and drinking water. Shell eggs and other metabolically active livestock products may also be treated. If livestock may be exposed to one or more residues of concern differing from those found in animals, then one or more additional livestock metabolism studies involving dosing with these residues may be required.

10. If there is a numerical tolerance or tolerance exemption level to enforce, then a residue analytical method suitable for enforcement purposes is required. The method must be supported by an independent laboratory validation.

11. If there is a numerical tolerance or tolerance exemption level to enforce, then testing is required to determine whether the Food and Drug Administration/United States Department of Agriculture multiresidue methodology would detect and identify the antimicrobial and its residues of concern, as part of programs to monitor pesticides in the U.S. food supply.

12. Data are required if an antimicrobial may be applied directly to water or if there is the potential that the antimicrobial-treated water could be used directly for drinking water purposes by humans or animals or that contaminated water could run-off, leach, or be discharged from treated sites or materials and make its way into potable water.

13. Data are required if an antimicrobial may be applied directly to water inhabited by fish or that will be inhabited by fish or if contaminated water could run-off, leach, or be discharged from treated sites or materials and make its way into bodies of water containing fish that may be used for human consumption.

14. Data are required if an antimicrobial may be applied directly to water used for irrigation of food crops or such that contaminated water could run-off, leach, or be discharged from treated sites or materials to make its way into water used for irrigation of food crops.

15. If the antimicrobial may be applied directly to livestock, metabolically-active livestock commodities (e.g., eggs), livestock feed or drinking water, or livestock premises, or a livestock metabolism study indicates that residues of the antimicrobial may result in livestock commodities, studies are required to determine the magnitude of the residues of concern in fat, meat, meat by-products, milk, poultry, and eggs that may be consumed by humans. These studies, however, may not be required in cases where the livestock metabolism studies indicate that transfer of pesticide residues of concern to tissues, milk, and eggs is not expected to occur at the maximum expected exposure level for the animals.

16. If food crops or raw agricultural commodities of food crops may be exposed to an antimicrobial, then residue studies are required to determine the magnitude of the residues of concern that may enter the human diet. Such exposures include, but are not limited to, postharvest fruit and vegetable treatments and application of antimicrobial chemicals to field crops, mushroom houses, empty or occupied beehives, or wood used to construct beehives.

17. Data on the nature and magnitude of residues in processed food or feed are required if antimicrobial residues could potentially concentrate on processing. If so, the establishment of a separate tolerance higher than that in the raw agricultural commodity may be required.

18. Data are required when dietary exposure values at the tolerance level or screening-level (high-end) result in estimates of dietary or aggregate risk that meet or exceed the Agency's level of concern. These data may include, but are not limited to, washing, cooking, processing, or degradation studies as well as market basket surveys for a more realistic residue determination. Protocols must be approved by the Agency prior to the initiation of the study.

Part 161 [REMOVED]

6. Remove part 161.